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Listerian Oration.[1]

THE PHYSICIAN AND HIS WORKSHOP.

By C. G. McDONALD,
Sydney.

THE great Lister, in memory of whom this oration was founded, was a genius of science. There is no good and complete definition of a genius known to me, but all men of genius seem to have this quality in common, that they can crystallize in one great work or discovery the experience of the age in which they live and anticipate the truth towards which their fellows of less clear vision are moving. Such a one was Dante, whose great work gives utterance to the complete spiritual and secular development of mediæval man; such was Shakespeare, who, animated by the spirit of the renaissance which worked in him as a leaven, set down, especially in the great tragedies, the truths of the drama of human life, combining a full knowledge of man in the past with a prophetic insight into his future; and such also was Joseph Lister, who in the narrower field of medicine integrated the surgical knowledge of his age with the great discovery of Pasteur and at one bound leapt to the goal towards which all others were groping.

No brilliant and dexterous operator, but a conscientious and careful craftsman in his handling of human tissue, Lister was nevertheless at the end of his career the greatest of all surgeons. He had that higher seriousness of great men of which Matthew Arnold writes, an intensity of feeling which finds immortal expression, whether it be in a great poem, a great painting or a great scientific discovery. Beside the men of talent who rubbed shoulders with him he seemed at first an unimpressive figure. The world appreciates men of talent because it understands their language, which is the symbolic declaration of its own ideas. It is slow to recognize the genius because he speaks with the tongue of a seer of things open to his vision which others cannot see. For many years Lister lived a life of intellectual isolation while his professional colleagues showed a hostile resistance to his enunciation of the "antiseptic principle". His deep conviction that he was right and his antagonists wrong at last won through, and towards the end of his life the world of science was pleased to rank him with Harvey and Sydenham.

I have chosen as the subject of tonight's address a review of the work of a physician as we see him in his consulting room or by the bedside in a hospital ward. I have done so for the reason that there is a tendency in these days to belittle the work of the clinician and to compare it unfavourably with that of the laboratory worker. I have heard physicians themselves speak slightingly of clinical work as having no scientific importance and being little more than a respectable means of earning a good living. There was a time when chairs of medicine were filled only by physicians of long clinical experience. Today it is the brilliant young investigator who has won renown in physiological or clinical research that is claimed for a medical professorial chair. This statement certainly applies to the large hospitals of London, where the old clinician as we once knew him seems to be dying out. These are the days when skill in experiment and the ability to reduce medicine as far as possible to pure science hold full sway. It will at once be granted that the change has meant much for the widening of our knowledge of the processes of disease. More

[1] Delivered at a meeting of the South Australian Branch of the British Medical Association on April 27, 1950. Received for publication May 6, 1951.

advances have come in a few decades out of clinical and laboratory experiment than in a century from mere clinical observation. But whereas among a multitude of experimenters those capable of making great and original discoveries are few, the physicians of distinction who can apply their art and knowledge to the immediate problems of disease are many. This is fortunate for the community, which depends on the clinician for the urgent relief of illness.

Now the value of the physician is not the mere sum of his training, knowledge, experience and manual dexterity. His highest quality—to use the words that John Brown, the author of *Horæ Subsecivæ*, was so fond of repeating—is "that power over what Plato calls the middle propositions which lie between exact facts and speculative knowledge and are concerned with immediate application and action". In medicine, as in all callings, as indeed in any scientific investigation that is worth while, inferences, estimates and judgements are made under the direction of mental processes which by their very subtlety defy scientific analysis. This "right judgement in ratiocination" or "illative sense", as Newman describes it, is the faculty which determines the excellence of a physician in diagnosis, or of a lawyer in cross-examination, or of a general in the disposition of his troops. It arises of course from education, training and long experience, which are capable of measurement, but in the storehouse of the brain these are activated by the mind as by a ferment. Sir Alexander MacCormick, one of the greatest surgeons Australia has known, had an illative faculty that was little short of genius. He was a good anatomist, he had dexterous and sensitive fingers, he had seen much good surgery in Scotland and England. But in knowledge, skill and experience there were many his equal. As a teacher he was inferior. He wrote but little and none of it was striking. Yet in diagnosis he was uncanny, knowing when to operate and when to stay his hand, although unable to say why, while in the theatre problems of the surgical approach to lesions and the best mode of their excision resolved themselves under the magic of his hands, and that meant the magic of his mind. Now few surgeons can emulate MacCormick and few physicians Osler, and a Sydenham or a Lister comes once in a century, but the general excellence of physicians and surgeons depends on their training in clinical schools and on their constant intercourse with patients in both hospital and consulting room. It depends also on their intellectual capacity, their enthusiasm or driving force and their command of the "middle propositions". For years I have watched successive house physicians come and go. Some enter the wards after graduation without enthusiasm. They are confused in the new *milieu* of a hospital ward now that they must assume responsibility for men and women who represent much more than the diagnoses with which they are labelled. Good students though they were, these young graduates seem nostalgic for the things they have left behind—the cadaver on the dissecting room table and the bottled specimens in the pathological museum. Others, and these are the choicer spirits, are transfigured by their new experience. Clinical medicine opens up for them vistas of adventure of which they had never dreamt. Their minds ignited as with a torch, they set out for lust of knowing on a much more golden journey than leads to Samarkand.

The good house physician has better opportunities of coming to close quarters with his patients than his chief, who visits them once or twice a week, and then only in company with the house physician and sister or a retinue of students. The house physician may see his patients privately and alone—an indispensable requisite for their full cooperation. Students who trail their clinical teachers into the wards get a false notion of what medicine is. They appreciate the stimulating discussions by the bedside on differential diagnosis and treatment, but their approach to the patient is impersonal in the presence of so many persons. Further, they see around them patients dying or only temporarily relieved of congestive cardiac failure and others with advanced nervous lesions for whom no cure is known, and they come to the conclusion that medicine when compared with surgery is a gloomy and ineffectual science. And they are right in their own fashion, for medicine as they see it practised in clinical schools is more of an intellectual exercise than a therapeutic triumph. It is only when they themselves enter general practice or become consulting physicians that they view medicine in its proper perspective. The relief of organic lesions in their early phases and the treatment of the neuroses, which form such a large proportion of the complaints of men and women, strike them for the first time as the real activity of internal medicine. Unhappily the young doctor is too often unprepared for a proper approach to these problems, and his future development as a physician is determined largely by trial and error.

He who would succeed in the practice of medicine must in the first instance have a sound training in the fundamental sciences, and especially in physiology, which is the basis of all biological study. In the wards and in the consulting room he must examine and reexamine his patients meticulously and with interest, so that he may grow familiar not only with the abnormal, but with the normal manifestations of the human body. Only a bad doctor grows weary of examining a healthy heart or testing a normal urine or trying to feel an elusive spleen. The physician who can proclaim the healthiness of a patient's body may exult equally with him who hears the veiled puff of Skoda over a cavity in a tuberculous lung. Good history-taking is even more important than physical examination. To know symptoms thoroughly is to be expert in medicine. Mackenzie's greatness lay not in his invention of that ungovernable instrument, the ink-writing polygraph, nor in his speculative hypotheses on the causes of abnormal cardiac rhythm, but in his profound study over many years of the medical histories of plain men and women in the little Lancashire town of Burnley. To know symptoms well is to know common diseases, and to know common diseases is to be a good physician. Have you ever felt a blush of shame on your cheek when a colleague tells you that he has recently seen two "cases" of *paramyoclonus multiplex* or three of the Waterhouse-Friderichsen syndrome, and dilates learnedly on these rare entities, oblivious of your discomfiture? Next time you meet him, rally your flagging powers by asking him what is the commonest cause of headache or whether he knows why an epileptic froths at the mouth, or if you wish to prove to him that you also are a pundit, at what level in the psyche (if the psyche has levels) are painful sensations cut off in cases of hysterical anæsthesia.

Another requisite for the good physician is an inborn generosity of mind, which displays itself in kindness to patients, tolerance of their foibles and sympathy with their fears. Intellectual pride is the shipwreck of many a young physician, as gentleness and humility are the salvation of others. "Police might be tyrants", said Sumner Welles, "if they had no political superiors", and he might have added that politicians themselves sometimes get drunk with power till they are sobered by an avenging defeat at the polls. "Few tricks of the unsophisticated intellect", said another American, Richard Tawney, "are more curious than the naïve psychology of the business man, who ascribes his achievements to his own unaided efforts, in bland unconsciousness of a social order without whose continuous support and vigilant protection he would be as a lamb bleating in the desert". Acton's famous tag, that power always corrupts, applies to medical men as much as to tycoons and princes, and the best antidote to this corruption is the humility that comes of our manifold errors and human weaknesses and the warmth of our sympathy for those whom it is our privilege to serve.

In the management of patients suffering from organic lesions it is often immaterial whether they are treated in hospital or consulting room. Translation of the patient to a bed in hospital is determined by the necessity of diagnostic facilities or of good nursing rather than by any greater skill which the physician can exhibit in hospital. The treatment of the neuroses, however, requires the atmosphere of the consulting room with two persons alone holding the stage—doctor and patient. The presence of another doctor or a nurse or worse still a relation destroys that unreserved candour of the two actors without which effective resolution of anxieties is impossible.

Every physician will admit that the neuroses form a large proportion of the conditions he is called upon to treat. In most instances he suspects the non-organic character of the patient's complaint on the history alone, for the reason that over many years he has studied symptoms carefully and he has learned to dissect those characteristic of organic disease from those that have a mental origin. Nevertheless he makes a careful examination of all systems before daring to express an opinion. To the majority of these patients the quiet but definite intimation that there is no organic lesion brings immediate comfort and relief. But it is not enough, for unless the patient has some rational explanation of the mode of development of his symptoms they will recur sooner or later after he departs from the physician's presence.

Every doctor knows, or should know, the physical symptoms of an anxiety state—the general feeling of ill-being, the churning sensation in the epigastrium, the pounding of the heart against the left breast, the loss of appetite and the feeling of distension or discomfort after meals, the tremor of the hands, the restlessness of the lower limbs, which cannot be composed into a comfortable position, the light-headedness on sudden change of posture, and the headache which is unrelieved by aspirin. He knows also from his own, if not from his patient's, experience, the tossing and turning in bed at night, the crushing down of worries from the field of consciousness, the ultimate passage into sleep and the quick reawakening with the anxiety again foremost in the mind. He knows that ultimately the patient succeeds in repressing the worry that besets him, but is now convinced that he is a sick man, with symptoms referred as a rule to a specific segment of the body or a definite organ, whether it be the heart in the guise of left pectoral pain and palpitation, the stomach in the form of fullness after meals and epigastric discomfort, the site of an appendicectomy scar in the shape of vague pains and colonic rumblings, the skull as headache, dizziness and loss of the power of concentration, or the muscles and fibrous tissues as vague aches and pains and tender spots. He knows that these symptom-complexes, now referred to as the visceral neuroses or psychosomatic disorders, are the result of a successful transfer of the patient's anxiety from the field of the mind to the field of the body. He may also know that these visceral neuroses have come into being because the patient has elected not to grapple with a problem which he finds it impossible or painful to solve and has unconsciously taken refuge in physical illness. He knows further that the neurosis is simply the original anxiety masquerading as an organic defect. He knows all these things, but too often he fails to remember that the patient does not know them and if he did would learn how to deal in future with the manifold situations of life which confront him. Even a problem which is impossible of solution loses its terrors once it is boldly faced.

The physical symptoms experienced by the patient suffering from a visceral neurosis awaken what might be called secondary fears. If the patient has pain in the left breast, palpitation and dizziness, he fears that he has heart disease, and when he retires to bed in the evening he is terrified that he may be found dead in the morning. If he has gastric symptoms his fear is of ulcer or cancer, and generally cancer. An older patient, afflicted with neurotic headaches, thinks them the forerunner of a stroke or, worse still, a tumour of the brain, and if, as often happens, he is confused in thought and affected in memory, he is afraid that he may go insane. All of these are terrors which to the physician are irrational, but to the patient most real and the cause of dreadful foreboding.

In his approach to treatment of the patient the physician is unwise if he seeks to probe at once the anxieties which originally harassed his patient before the occurrence of the psycho-physical transfer. It is much better for the physician to talk broadly of the mechanism I have just outlined. The patient will quickly recognize that it is he himself who is being described, and if the physician speaks with understanding the patient will himself, unasked, reveal the worry which is disturbing him.

Occasionally it is necessary for the physician to withhold his sympathy and be severe with his patient, to brush aside his symptoms as of no account and to accuse him of a flight from reason. Let me quote the instance of a young woman who had symptoms referable to the gastro-intestinal tract—ill-defined pains in the lower part of the abdomen, nausea, vomiting and occasional mild diarrhœa—diagnosed by one doctor as due to colitis, by another as caused by abdominal adhesions, and by a third as the result of pancreatic insufficiency. She had been married but six months and had taken ill during her honeymoon. Although attracted to her husband in every other way, she had a profound distaste for the physical relations of marriage and her illness had released her from her embarrassment. Her spouse, who was an analytical chemist, had studied her symptoms in detail, and after conning many medical books had written a long dissertation upon them. She had come into my consulting room armed with this, with those innumerable X-ray films the sight of which makes every physician groan, with pathological reports of every description, and for good measure a notebook containing excerpts from medical articles collected by her husband to assist the doctors in coming to an opinion. Can you blame me if, after taking her history and performing a physical examination, I refused to look at the X-ray films and the other accessories, and after explaining to her as best I could why and how her symptoms were brought about, I told her sharply that unless she confronted her difficulties and ignored her symptoms her husband would ultimately weary of her and cast her aside, even though now in the first flush of affection he showed only too full a measure of devotion? On her next visit to me she told me smilingly that she was now quite well, but that her scientific husband seemed to have had a big interest taken out of his life.

There is often a striking contrast in the attitudes of patients who present with definite organic disease and those who suffer from functional nervous disorders. The former tend to understate their symptoms and recount them with a sang-froid and nonchalance that almost suggest boredom. A man of sixty notices a few glands in his neck, axillæ and groins and reports to his physician because his wife insisted. He is found to have a big spleen as well as enlarged glands, and a blood slide reveals the picture of chronic lymphoid leuchæmia. On the other hand, the neurotic patient tells you that his is a long story, asks you if he shall start from the beginning, and reinforces his memory by reference to what Axel Munthe called *le petit papier*. When he is being examined he has difficulty in localizing his pains and lavishes on their description a wealth of fantastic imagery. Occasionally he is made of sterner stuff and wants you to do the talking. He asks for a "thorough overhaul" and when you gently suggest taking a history first he is resentful, because he believes the recital of his symptoms will lead you to make the diagnosis which he fears to hear.

Patients afflicted with the visceral neuroses have symptoms of infinite variety, but they all have fear of common but dreadful things—cancer, strokes, paralysis, clots of blood, insanity, heart disease or a torn abdominal viscus. A trivial injury at work or play sustained by a man troubled at the time by some mental conflict may precipitate the onset and determine the location of the psychosomatic disorder. There are three parts of the human body which, when injured, provoke the development of symptoms which have no organic basis but are referred to the site of injury: the skull, the back and the left side of the chest. All men have an inherent fear of injury to the brain, the spine and the heart, and this dread is often reinforced by the solicitude of friends who always know of someone who after a similar accident died of a clot of blood on the brain or was paralysed for life or became a cardiac cripple. Unhappily the patient's apprehension is sometimes confirmed by his medical attendant, who fails to recognize the mental origin of the symptoms and assumes organic damage to exist when there is none. The good doctor in these circumstances is not he who demands skiagrams, electrocardiograms and other aids to investigation, but he who makes up his mind on the spot and dissipates with a vigorous expression of his opinion the terror that besets the patient's mind. When you hear

a physician speaking without reserve of such vague entities as "primary cardiac overstrain", "myocarditis", "the effort syndrome", "neuro-circulatory asthenia", "the post-concussion syndrome", "myositis", "fibrositis" and "auto-intoxication", you may safely infer that he has no grasp of the "middle propositions".

Perhaps the best observers of the human mind in its working are good general practitioners, who, gaining the respect and confidence of their patients, passing freely into and out of their homes and knowing intimately their social and economic conditions, are able to observe over many years the reactions of mind and body to anxiety. Were this study their only function they would not be good psychologists, but as their primary duty is the diagnosis and relief of physical illness, they can sift their observations with a shrewdness and judgement not always given to the specialist. Theoretical and experimental psychology, as taught in the universities, has its place in the study of the human mind, but is limited because it is largely based on hypothesis and tests performed in an unnatural environment. Who can strip the curtain from the soul in lecture hall or laboratory? The mind of man, which ranges beyond the flaming ramparts of the world, eluded Lucretius and eludes us all. But by the bedside or in the consulting room it is given to us to lower the barriers and to gaze with awe on some of the arcana of the mind. It is said that the objective of a good legal advocate is to expose the hidden motives of men; one of the duties of a good physician is to recognize and relieve that common interplay between mental and bodily function which is the cause of so much personal distress and social unhappiness.

We have all of us heard the common gibe that medicine is merely a technical occupation, devoid of the cultural value attaching to humanistic studies. Nothing is farther from the truth. The traditions of modern medicine extend back to the days of Hippocrates, when physic flourished on the island of Cos and outstripped in culture other branches of learning, and if we trace the earlier history of our craft our gaze will range over Sumerian, Egyptian and oriental medicine till it is lost in the twilight of antiquity. If by culture, if by humanism, we mean those studies that touch the strength and foibles and the despairs and aspirations of men, there is, rightly understood, a greater cultural education in a few years' practice of medicine than in a life-time devoted to the stilted and uninspired study of a foreign language. At a university conference which I attended at Oxford two years ago I heard learned professors representative of arts faculties in many parts of the Empire deploring the ignorance of medical and engineering students. They put their heads together to decide how many lectures on the humanities should be given to these young technicians to improve their culture. All went well till one professor castigated engineers and architects as particularly ignorant classes of men, who dealt with lengths of timber and tons of concrete and machines that offended the quiet of day. Mere robots of the lower order, they worshipped the centimetre-gramme-second system as their god. They traded in dead things. An elderly delegate jumped to his feet and announced with tremulous but clear voice that he was both an engineer and an architect and that the last speaker's conception of these professions was not his, that the bridges which spanned harbours and rivers and the spires of churches that pointed like fingers to the sky were products of the minds as well as of the hands of men, and that when architects built homes, however simple, and engineers worked in factories, however humble, or went down with miners into the earth, they shared as much in the drama of human life and came as close to the vibrating hearts of men as any humanist seated in a professorial chair. Therein he spoke for every professional man. The doctor is apt to forget the cultural value of his work just as he is prone to under-estimate his power over the lives and destinies of his patients. It takes several years to train a skilled tradesman, but half the span of a man's life to make him a good doctor. After six years spent in university laboratory or hospital ward, armed though he be with his bachelor's degree, he has neither the skill nor confidence to practise unaided the difficult art and science of medicine. This skill and confidence, for which no diploma can be granted by university or Royal college, will come as the result of application, experience and the repeated exercise of those mental and spiritual qualities which are the real armamentarium of the professional man. In the broad laboratory of practice in which he will work and learn till he dies, he will find that medicine is no mere technical vocation, but an applied science exercising his highest faculties and concerned with problems which demand depth of thought, ability to profit by the variations of experience and at least some fertility of imagination.

Nevertheless we owe it to our patients and to ourselves to widen our vision of this mysterious world and our knowledge of its storied past by deep and general reading. Better, it is true, that we should be good doctors than bad scholars, but when the long day's task is done our minds may feed on the broad pastures of general scholarship and thereby be enriched. It matters little what we read so that we do it both for pleasure and profit. He whose ear is attuned to the nuances of language will find in poetry a never-ceasing source of joy—poetry which according to Aristotle is truer than history, poetry that is still fresh and fragrant after endless repetition. But the muse of Helicon is not for us all. Philosophy, archæology, history, biography, the novel, prose in any form, the study of a foreign language—any or all of these may constitute for us that mental nourishment that is known as a liberal education. You have perhaps observed the ever-increasing devotion of the young and the not-so-young to music. The study of music in its theory and its history is an intellectual exercise and its reward comes in a deep appreciation of the higher emotions of man. But when young folk crowd into drawing rooms and under low lights and with rapt looks on their faces listen to a concerto of which they have little intelligent knowledge, I wonder if they are not seeking a mental nirvana.

In his thoughts on the present discontents the doctor may well fear not only for his country, but for the future of his own profession. The times are out of joint. A victorious war has yielded place to a disastrous peace. In Pitt's phrase, the lamps of Europe which indeed went out one by one during the second world war have not yet been relighted, and the lamp of England, our own mother, flickers fitfully. We know only too well that the wounds of Europe are our wounds—two great wars have taught us that—and no world disaster leaves us unscathed. Every thoughtful young man or woman must fear deep in his heart that his just heritage may be wrested from him. The planning of his career seems a mockery. He knows not if or when or how a third world war will swallow him up. Nevertheless to despair is to undergo atrophy of the spirit. But a year or two ago doctors in this country were threatened with nationalization of their profession, which to them meant loss of freedom. They held together and went on with their work. And they won through. They proved that the integrity of medicine rested with those who practised it, not with the planners and the doctrinaires. And what we have done you may be sure the whole nation is doing. Good times will come again, even if slowly, even if in less abundance than formerly.

But we cannot afford in the flush of our success to ignore developments that impinge directly on our work. At the beginning of this century there were few medical or surgical specialties and medical men set about their tasks with none but nurses to help them. The day of biophysics and biochemistry had not yet come and there was some justification for Osler's reference to "the simple study of medicine". Now it is a different story. Physicians and surgeons have not only divided much of their work into specialties, but they have also enlisted the services of ancillary professions which specialization has brought into being. And so we have almoners, social workers, dietitians, physiotherapists, occupational therapists and biochemists, not to mention technicians in radiography, radiotherapeutics, pathology, bacteriology, and so on. It would be idle to deny that we have not always hastened to take these bodies of men and women under our wing. Perhaps this is for the best, for doctors, traditionally conservative, yet in matters that concern the welfare of their patients generously elastic, must be persuaded that any new move-

ment is for the good of the sick under their care. And so in the last few decades great developments in social work have evolved, often without our help or benediction. Gradually, however, as it becomes evident that qualified social workers, whether they be almoners in hospitals, nurses in tuberculosis dispensaries, occupational therapists or social officers in institutions or factories, have as their aim the bodily and mental good as well as the economic and social happiness of mankind, we have become more lavish with our help. Perhaps in the near future almoners will participate in the teaching of social medicine to medical students, as was urged so earnestly in the Goodenough report. The physician treating patients in public hospitals often knows little or nothing of the homes from which they come, or of the storms of life through which they have passed. If he did he would understand better the physical and mental wreckage of some of the patients under his care. Not to inquire into these things is to be satisfied with a half-truth.

I hope that I have made the drift of this address clear. It is in brief that the practice of medicine is no mere technical procedure; that a physician is known and honoured not by the knowledge that comes to him, but by that measure of wisdom that lingers. He sees his patients in his consulting room or by the bedside and yet his real workshop is his own mind—that mind the complex processes of which, born of innumerable experiences, baffle its own understanding, that mind which is its own discipline and its own power and on this earth its own reward. Our Royal Australasian College of Surgeons has a grand motto on its coat of arms: "The torch of the mind is the kindler of glory." Its sister college has a simpler legend: "To serve the health of men." The two are complementary one to the other, for our greatest glory is to obey the Hippocratic injunction to preserve from harm that human body which is the temple of the mind. We who play with the forces of birth and life and death should simultaneously be proud of the task to which we are called, and abashed at the disproportion between its immensity and our restricted powers. The good physician seeks no high place in the councils of men, but, like Zinsser, is supremely happy so long as he can "remain close, heart and hands, to the problems of disease".

TUBERCULOSIS OF THE LIVER: INCLUDING A REPORT OF FIVE CASES.

By D. G. NEILL,
Brisbane.

MORE than academic interest is attached to the diagnosis of rare diseases, for the patients are just as much in need of attention as others, and as medical knowledge increases more and more of the rarities become susceptible to treatment. Particularly is interest called for in the diagnosis of rare forms of tuberculosis, and for this reason it was thought desirable to review the subject of tuberculosis of the liver and to give clinical and pathological notes on five cases, with discussion of some of the pathological features.

Review of the Literature.

Rolleston and McNee in 1929 described in their book two cases of tuberculomata of the liver and cited 14 from the literature (Moser, 1946). In Australia, de Crespigny and Cleland (1923) reported autopsy findings of multiple tuberculomata of the liver associated with a degenerated hydatid cyst in a man aged thirty-six years, and Webster (1938) gave an autopsy report on a girl aged eleven years, who also had a trichobezoar. In America, Harrell and Simpson (1938) reported a case of recurrent hyperpyrexia due to a solitary tuberculoma of the liver, the third solitary lesion found described, and Moser (1946) reported a case of multiple tuberculomata of the liver with calcification producing X-ray opacities.

The disseminated form of tuberculosis of the liver, with miliary tubercles chiefly in the portal tracts, is usually described as part of generalized hæmatogenous tuberculosis. Yet although healing with fibrosis may occur (Rubin, 1948), not many references to diffuse hepatic fibrosis resulting from tuberculosis are found. Karsner (1942) records that certain authorities regard tuberculosis as a possible cause of Laennec's cirrhosis of the liver, but does not himself accept the view as final. Writing of pericellular or syphilitic fibrosis, Hurst (1946) mentions tuberculosis to be considered when the Wassermann test produces a negative result and other signs of syphilis are absent. No recent case reports have been found.

Tuberculous cholangitis, associated with tuberculous cavities in the liver, has been studied and described by Winternitz in 1908 (Karsner, 1942) and by Morley Fletcher in 1899 (Bland-Sutton, 1910).

Pathology.

Three types of tuberculous infection of the liver are described: disseminated miliary tuberculosis; conglomerate tubercles, including tuberculomata; and tuberculous cholangitis. All are forms of tissue reaction to the organism *Mycobacterium tuberculosis*, modified by the variable factors of organism virulence and host resistance.

Disseminated miliary tuberculosis is usually seen in an acute form, resulting from the entry into the blood-stream of very large numbers of organisms followed by their arrest in the liver and other organs. That the human liver tissue possesses relatively good defences against invasion by the organism of tuberculosis may be inferred from the invariable involvement of liver in miliary tuberculosis and from the rarity of finding later extensive lesions (Rich, 1944). When, in spite of these defences, miliary tuberculosis of the liver occurs, the illness usually soon ends in death. The histological appearance of a typical miliary tubercle—central caseation, epithelioid cells, multinucleated giant cells and peripheral lymphocytes—is well known. In the liver, however, often there may be found only atypical tubercles with little or no caseation and very scanty giant cells (Boyd, 1944).

Chronic disseminated tuberculosis undoubtedly occurs in other organs, and some workers are satisfied of its occurrence in the liver. Instead of complete resolution, which may sometimes follow the acute disseminated form (Illing, 1945), it is believed that occasionally healing with fibrosis may occur. The healing may be complete or it may localize a number of scattered, partially fibrosed tubercles containing living but relatively inactive organisms. The difficulty in distinguishing such a condition from diffuse hepatic fibrosis of other origin need scarcely be mentioned.

Conglomerate tuberculosis may result from the survival, extension, and coalescence of tubercles in a varying number of parts of the liver, solitary lesions being very rare. Sometimes irregular caseous abscesses are formed, but often the lesions are rounded, with a firm fibrous capsule, and because of a resemblance to a tumour have been called tuberculomata. They may remain small or attain a large size. Central softening may occur. Histological examination typically reveals caseation in the middle, with epithelioid cells and a few giant cells at the margin, the whole enclosed by fibrous tissue. Resemblance to a syphilitic gumma may be complete and may require other methods of differentiation (Boyd, 1944; Ogilvie, 1943). Calcification may occur in the necrotic tissue after a time; but the presence of calcification does not necessarily indicate complete inactivity (Rubin, 1948). Instead of localization by fibrosis and calcification, the balance of power may pass for a time to the organism, and spread to a varying extent may occur directly or by way of bile, blood or lymph channels.

Tuberculous cholangitis or pericholangitis may follow spread from the perilobular connective tissue into the bile ducts, or, more rarely, upward extension of tuberculosis of the extrahepatic bile ducts. Bile-stained, cheesy material is then found in tubercles of varying size.

Primary infection elsewhere, almost always in a lung or part of the alimentary canal, must precede all tuber-

culosis of the liver, except possible traumatic infection; but healing may make the primary site difficult or impossible to recognize. Spread to the liver may occur from the primary site or from some secondary focus.

Clinical Features.

Frequently signs and symptoms of hepatic tuberculosis are few or absent. Recurrent hyperpyrexia may be the only abnormality. Sometimes, however, symptoms of toxæmia from an abscess may be severe. Liver enlargement may or may not be detectable. Occasionally pressure on an important neighbouring structure, such as a large bile duct, may lead to secondary signs and symptoms. Only if there is very extensive liver involvement will there be noticeable interference with liver function. It is not possible to deal in detail with these clinical possibilities, but it is important to appreciate that involvement of the liver is usually one inconspicuous aspect of the disease process, and other clinical features may predominate.

Diagnosis.

Diagnosis of the disease to which treatment can be directed is of great importance, and most of this section deals with laboratory proof of diagnosis. Suggestion of the diagnosis may be obtained from clinical points, opacities revealed by X rays or findings at operation and biopsy. Proof is a more difficult matter, but must be attempted.

The diagnosis of tuberculosis is only presumptive when based on histological grounds without isolation and identification of the responsible organism, because it has been shown that a number of other conditions—syphilis, leprosy, *lymphogranuloma venereum*, tularæmia, to name only some—may produce at times appearances similar to those of tuberculosis (Anderson, 1948). Some reference to these similarities is made in the discussion of cases, particularly Case I. The need for supplementary bacteriological investigation in order to prove the diagnosis becomes obvious.

The matter is complicated by possible variation from the usual in the reaction of the tissues to the *Mycobacterium tuberculosis*. The organism has been isolated from numbers of cases in which non-specific inflammation was present, and in a symposium on the diagnosis of tuberculosis McDonald and Weeds (1950), of the Mayo Clinic, referring to this variable tissue response, write as follows: ". . . the extreme degrees of variation are not uniformly appreciated by those responsible for making histologic diagnoses." They adduce convincing histological and bacteriological evidence of the variation. Such cases cannot be diagnosed and may not be suspected without bacteriological investigation.

Negative results on bacteriological examination can never, of course, exclude a condition, particularly if the examination is performed only once. Insufficient or unsuitable material and inhibition by a drug are examples of what may contribute to a negative cultural finding. In a case presenting histological indications of tuberculosis a negative cultural finding or negative results on animal inoculation only fail to confirm the diagnosis, which then remains presumptive.

The great value of histological examination needs no defence and is properly well appreciated, and it is not lessened at all by this equally proper emphasis on bacteriological methods. For best results in diagnosis, forces should be combined and all available information gathered.

Fresh tissue should be divided into parts for each type of examination. Formalin fixation is preferred for the routine histological study, but alcohol fixation of another portion of tissue followed by new fuchsin staining of paraffin sections is recommended by Fite (1938) for the demonstration of acid-fast and alcohol-fast organisms. Direct smears and cultures, such as microslide cultures (Pryce, 1941) in Youman's medium (Youman, 1944), should be prepared and guinea-pig inoculation should be carried out from the other tissue and exudate after suitable treatment, for example, with trisodium phosphate. In addition to routine hæmatoxylin-eosin staining, tissue sections are stained with Ziehl-Neelsen and Giemsa or Gram stains in the search for organisms. Gram and Ziehl-Neelsen stains with or without auramine methods are used for staining smears. Occasionally, as in Case I, skin testing of the guinea-pigs with tuberculin may be found useful, for by injecting single organisms Bretey (1944) has found tuberculin sensitivity to develop without generalized tuberculosis. With the exception of alcohol fixation these methods have been employed when practicable in the four recent cases.

Treatment.

Treatment of individual patients must be left to specialists in possession of full information. But the recovery from very severe illness following surgical treatment in two cases (Moser, 1946; Harrell and Simpson, 1938), and the prevention or treatment of complications by modern drugs, make for a more optimistic outlook.

Reports of Cases.

CASE I.—S.M., a pork butcher, aged fifty-nine years, was admitted to the Brisbane General Hospital on October 28, 1945, because of a constant pain in the right side for four or five weeks. The pain radiated to the back. A tender mass was felt in the right upper quadrant of the abdomen and the liver was enlarged over three fingers' breadth below the costal margin. Laparotomy on November 9 revealed multiple, yellowish, hard masses in the liver, thought to be secondary neoplasms. A mass at the hepatic flexure of the colon was adherent to the liver and adjacent to a small abscess, and enlarged glands were felt over the pancreas. Post-operative pyrexia lasted three days. A biopsy of a rounded liver nodule revealed necrosis and fibrous replacement without any trace of the original liver tissue. Diverticulosis had been found and the mass was then considered to be an abscess following diverticulitis. The patient was discharged from hospital on December 7, 1945, without a diagnosis of the liver condition.

His second and final admission to hospital took place on June 28, 1950, because of tenderness in the buttocks following an accidental fall six days previously. He had felt "out of sorts" for a year. For four years he had had no abdominal pain but had lost weight. He had a small epigastric scar in the place of an old discharging abscess, and a small discharging fistulous opening about eight centimetres to the right of the umbilicus, both of which had developed after the operation. His urine had been dark for three or four months.

Examination of the patient revealed slight jaundice, a few telangiectases, a non-tender enlarged liver, and severe bruising of both buttocks with a small ulcer on the right. Ascites and distended veins around the umbilicus were noticed. The fæces were pale. The icteric index was 17 and the cephalin cholesterol flocculation test produced a positive result (++) in forty-eight hours. The bleeding time and the prothrombin time were normal, but the coagulation time was prolonged—seventeen, twenty and twenty-two minutes on three separate days. The hæmoglobin value was nine grammes per 100 millilitres of blood and the erythrocytes numbered about 3,000,000 per cubic millimetre.

Incision of a perianal hæmatoma was performed on July 6, 1950, and about 150 millilitres of material were removed from it. Considerable bleeding from the site nine days after operation necessitated a blood transfusion, whereupon the hæmorrhage ceased.

The serum protein content was estimated at 6·7 grammes per 100 millilitres, but the albumin content was reduced to 2·3 grammes per 100 millilitres and the globulin content was increased (4·4 grammes per 100 millilitres). A glucose tolerance test produced a rise from the fasting blood sugar level of 96 to 171 milligrammes per 100 millilitres after one hour, 148 milligrammes per 100 millilitres after two hours. Radiotherapy was given for a basal-cell carcinoma on the upper lip. Scattered areas of calcification in the upper part of the abdomen were seen on X-ray examination.

After a month a slow transfusion of 1·5 litres of blood was given and liver needle biopsy was performed under local anæsthesia. The biopsy yielded only a little amorphous white and then yellowish material, examination of which gave negative results except for growth of a coagulase-negative staphylococcus and the recognition of bile in the necrotic tissue.

A low-grade fever developed after the blood transfusion and persisted for six weeks after the liver puncture, in spite of massive doses of penicillin for the first fortnight. The patient's temperature fell to normal after the six weeks

and remained so until his death. The Mantoux test produced a positive result, the Casoni test a negative result.

Œdema and ascites increased, and *paracentesis abdominis* on September 14 yielded 4·7 litres of fluid, which was yellow and slightly turbid, and contained numerous polymorphonuclear leucocytes and 3·6 grammes of protein per 100 millilitres, but was sterile on investigation with ordinary culture media. Cramping abdominal pain occurred a week later, and

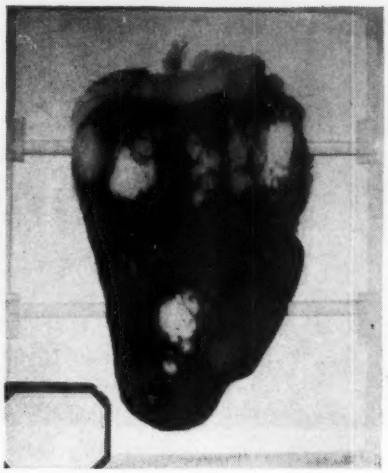

FIGURE I.
Case I. Showing rounded fibrotic and irregular caseous nodules in the liver. The liver tissue is stained Prussian blue.

impacted fæces were found and partly removed. The pains ceased, but the patient became progressively weaker. At 6 a.m. on September 28 he complained of having had a

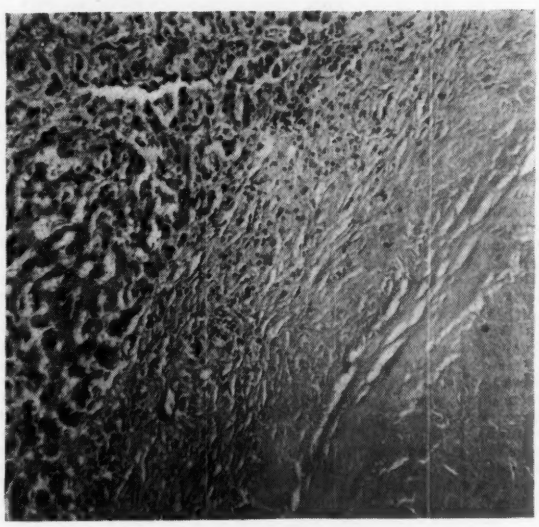

FIGURE II.
Case I. The margin of one rounded nodule in the liver (x 85).

bad night, and an hour later he became cyanosed and gasped for breath; he died with coffee-ground type of vomitus running from his mouth and nose.

Four hours *post mortem*, examination showed the subject to be a thin, pale man with ascites and œdema of moderate degree. Body hair was absent. Both abdominal and perianal scars were cleanly healed. The external openings of both fistulæ were occluded by thin scars, about three millimetres in diameter. Internally, a thick-walled track passed from the right fistula into an abscess in the liver, and a similar track passed from the epigastric fistula to end in dense adhesions over the middle of the lower part of the anterior surface of the liver. Approximately a gallon of clear yellow fluid was free in the peritoneal cavity.

FIGURE III.
Case I. Liver, pancreas, superior pancreatic lymph glands, duodenum and spleen, showing the caseous foci in liver, lymph gland and spleen.

The liver was enlarged, weighing two kilograms. It was dark reddish-brown in colour, and gave an immediate strong Prussian-blue reaction for iron. Fine nodularity was associated with diffuse fibrosis. Scattered through both lobes were a number of small, round, hard, white nodules, which varied in size from about two to twelve millimetres in diameter. Inspection of the cut surface of these nodules revealed white or white and yellow laminæ of dense fibrous consistence, with calcification of varying amount in the middle (Figure I). In addition to these very hard nodules other irregular-shaped foci of an apparently chronic inflammatory nature were scattered through the liver, particularly the right lobe. Some were white, others pale yellow. Some were caseous but firm; a few were very soft. Some tended to roundness and were about 1·2 centimetres in diameter, but some were about two or three millimetres in diameter and were clustered together in irregular groups (Figures I and III). Lying postero-laterally in the right lobe, an abscess cavity about three centimetres in diameter contained thick, yellow, fluid necrotic material, and was closed laterally, except for the fistula, by peritoneal adhesions. The gall-bladder was thick-walled and contained normal bile but no stones. The duodenum was firmly adherent to the lower surface of the liver, about two centimetres medial to the gall-bladder. The colon was pulled up to the liver by omental adhesions, but the bowel itself was not in direct contact.

In the middle of the spleen, which weighed 280 grammes, was an irregular cavity filled with soft yellow necrotic matter (Figure III). The margin was thin but rather firm and cream in colour. The rest of the spleen was dark and of normal appearance.

Superior pancreatic lymph glands were enlarged in size (up to 2·5 centimetres by 2·0 centimetres by 0·5 centimetres) and reddish-brown in colour. Two on the right contained small yellow caseous nodules, some of which had coalesced (Figure III). An enlarged anterior mediastinal lymph gland was also reddish-brown and gave a reaction for iron.

A very small, irregular ulcer, about two millimetres in diameter, was present in the upper part of the duodenum, right next to the pylorus, and two ulcers, each about three millimetres in diameter, were situated about three centimetres distally on opposite sides of the lumen, which was greatly narrowed there by a thickened ring of submucous connective tissue. The ulcers were shallow and contained yellow material. The edges were quite irregular and rimmed by dark altered blood pigment on reddened mucosa. Proximally, the duodenal mucosa was smooth. Only a little gastric juice and altered blood was found in the stomach and duodenum. No ulceration was found in the rest of the bowel, but the lower part of the jejunum and the ileum contained a moderate quantity of dark pigment like altered blood mixed with fluid fæces. In the colon and rectum the fæces were pale. Colonic diverticula were present but none was inflamed.

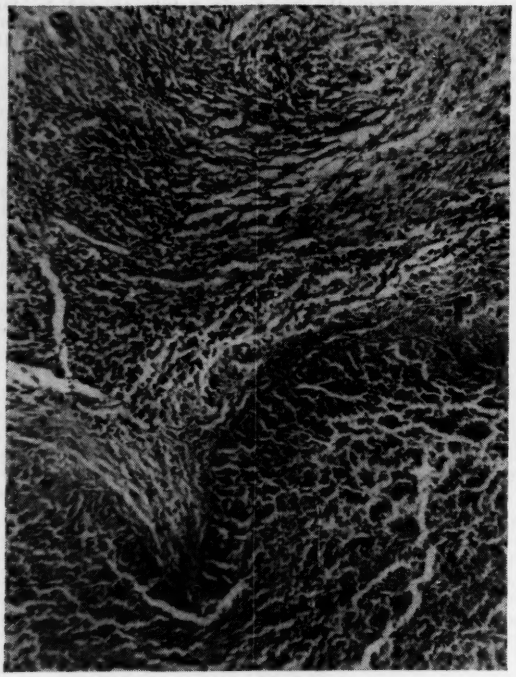

FIGURE IV.

Case I. Margin of one typical caseous part of the liver, showing granular necrotic material in the lower part, with very little fragmented chromatin, surrounded by palisaded epithelioid cells passing into loose connective tissue with chronic inflammatory cell infiltration (× 85).

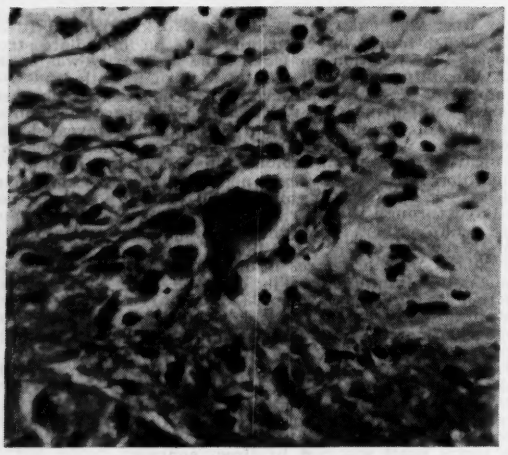

FIGURE V.

Case I. Higher magnification of the multinucleated giant cell and its surroundings in Figure IV (× 390).

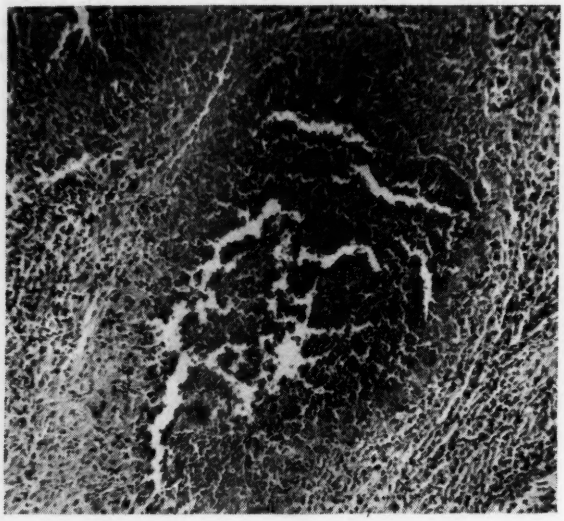

FIGURE VI.

Case I. One of the sections of liver showing accumulation of polymorphonuclear cells in the necrotic matter, surrounded by palisaded epithelioid cells and chronic inflammatory tissue (× 85).

Examination of the respiratory tract showed evidence of terminal inhalation of vomitus, a few specks of food, streaks of mucus, and much dark blood pigment similar to that in the stomach. The lung bases were congested. Each pleural cavity contained about 200 millilitres of clear yellow fluid. Small apical scars were present and the base of the right lung was firmly adherent to the diaphragm.

No significant abnormality was found in the other organs.

Histological examination of sections showed the firm white nodules to resemble the previous biopsy material in having a rounded aggregation of dense hyaline fibrous tissue and a variable amount of enclosed amorphous necrotic material, surrounded by a thin layer of chronic inflammatory granulation tissue (Figure II). The granulation tissue was not very vascular, mainly fibrous tissue, and merged into the surrounding liver cells, in which were visible large amounts of hæmosiderin. Calcification had occurred in some of the central necrotic material. The softer yellowish foci contained centrally a variable amount of necrotic debris, and peripherally a radial type of arrangement of the innermost epithelioid cells, numerous lymphocytes, a few plasma cells, an occasional giant cell, and a merging of the outermost epithelioid cells with the adjacent connective tissue (Figures IV and V). In most necrotic parts either no nuclear fragments or just fine chromatin particles remained. In an occasional place numbers of polymorphonuclear leucocytes were recognizable amongst the debris and appeared to outnumber fragmented mononuclear cells (Figure VI). An occasional necrotic area contained a little bile. Diffuse fibrosis of the liver was most pronounced around the portal tracts and was associated with large accumulations of hæmosiderin in the connective tissue as well as in Kupffer cells and parenchyma. Corresponding to the absence of coarse nodularity, there was only slight to moderate destruction of lobular architecture.

The irregular yellow lesions in spleen and pancreatic lymph glands were of similar chronic inflammatory structure to those in the liver. Large deposits of hæmosiderin were present in the glands.

The duodenal ulcers appeared of the acute inflammatory type, and contained large numbers of polymorphonuclear leucocytes. But under the distal ulcers the stenotic ring was caused by thickened submucous tissue composed of loosely interlaced collagen fibrils with a considerable amount of fibrinoid degeneration (Figure VII).

In the lung, aspiration of vomitus was confirmed. Examination of the apical scars and thickened pleura revealed only fibrous tissue with small numbers of lymphocytes.

FIGURE VII.

Case I. Section of the stenotic ring of connective tissue in the duodenum, showing the acute ulceration with numerous polymorphonuclear cells on the right, and the base of the mucosal layer on the left, where it is displaced at right angles to the line of the duodenum (× 85).

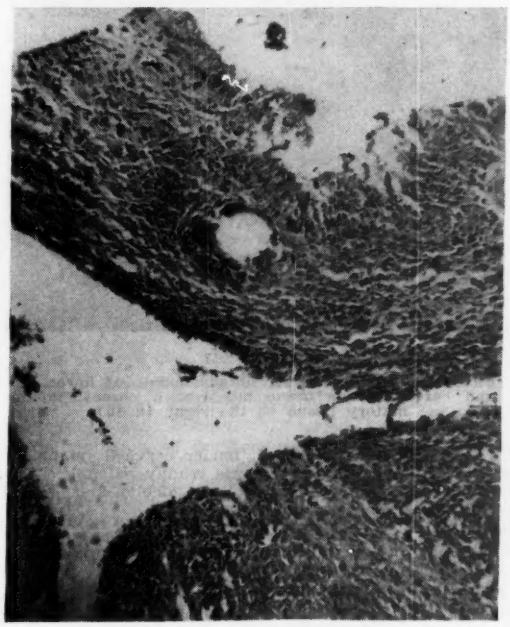

FIGURE VIII.

Case I. Section of cutaneous fistula, showing at the top palisaded epithelioid cells and giant cells at the edge of a tubercle, from which some of the necrotic tissue and parts of the giant cells have broken away (× 85).

The wall of the cutaneous fistula appeared in section as cellular fibrous tissue passing into epithelioid cells arranged radially around an area of necrosis (Figure VIII).

Ziehl-Neelsen staining of the paraffin sections of liver revealed only three acid-fast and alcohol-fast organisms resembling *Mycobacterium tuberculosis*, and six in one duodenal ulcer. But in a smear from the fibrin clot in the small residue of ascitic fluid two similar organisms were discovered, and a number were found, though not deeply

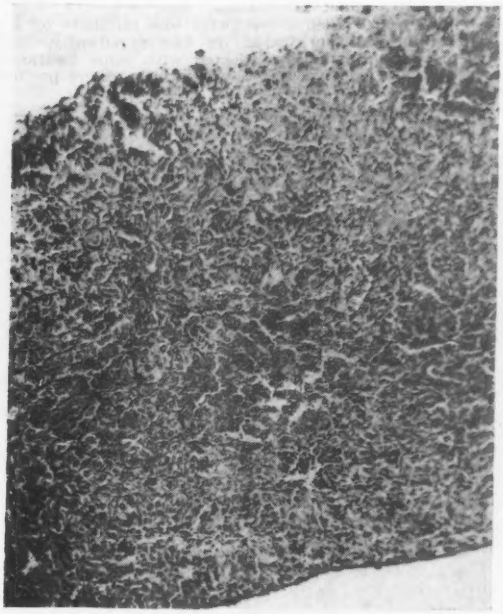

FIGURE IX.

Guinea-pig: liver tissue, showing necrosis in the top right portion, and polymorphonuclear infiltration, with many eosinophile cells, round it and in neighbouring parts (× 85).

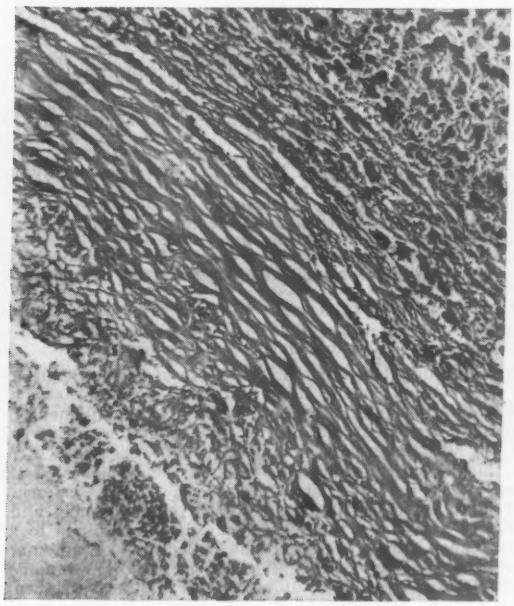

FIGURE X.

Case III. Liver, showing collagenous fibrous tissue and chronic inflammatory tissue around the necrotic middle (× 85).

stained, in smears made from the centrifuged deposit after a large quantity of caseous material had been dissolved in antiformin. Auramine O staining of a smear of this same deposit was followed by the finding of fluorescent organisms under the ultra-violet microscope.

After ten weeks a skin test with one millilitre of 1:1000 old tubrculin was performed on the apparently healthy guinea-pig which had been injected with some ascitic fluid. The test gave a positive result, while three others performed

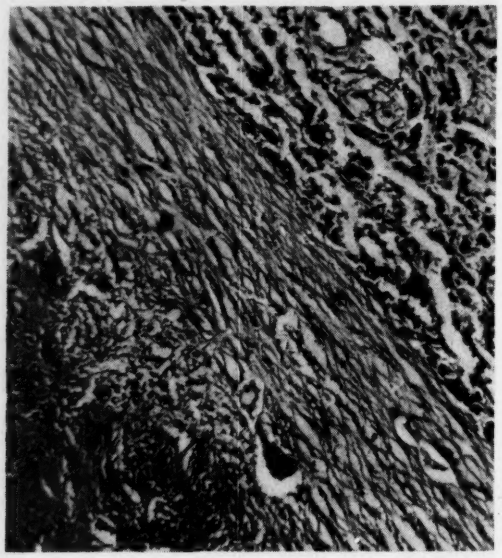

FIGURE XI.

Case II. Liver, showing two giant cells in the chronic inflammatory and fibrous tissue which surrounds necrotic tissue (× 85).

on the same day gave negative results. Two weeks later a test with 1:100 old tuberculin also gave a positive result, with an area of induration 12 millimetres in diameter. Ten days later the guinea-pig was killed, and two tiny, pale, whitish nodules were visible on the surface of the liver. Histological examination of sections of this part of the liver revealed some tissue necrosis with surrounding inflammatory infiltrate (Figure IX); the cells were mostly polymorphonuclear leucocytes, and these mostly eosinophile. Slightly increased fibrous tissue was present at the edge of the necrotic area and around neighbouring portal tracts. Finally, in two Ziehl-Neelsen stained sections of the guinea-pig's liver were found six acid-fast and alcohol-fast organisms which morphologically resembled *Mycobacterium tuberculosis*.

Giemsa staining of tissue sections gave negative findings.

Blood and cerebro-spinal fluid were removed at autopsy, and neither reacted to the Wassermann test.

Great clinical interest in the cause of the multiple areas of calcification in the liver and their possible association with the patient's chronic illness was supplemented by great pathological interest in the histological structure of the lesions revealed at autopsy. The resemblance to the tertiary lesions of syphilis was in some places striking, but the irregular extension of the liver lesions, the irregular necrosis in neighbouring lymph glands, and the negative results to the Wassermann test combined to make that cause very unlikely. The collections of polymorphonuclear leucocytes in areas of necrosis surrounded by radially arranged epithelioid cells or histiocytes resembled the lesions described in *lymphogranuloma venereum*, but that particular microscopic appearance was not considered diagnostic and the macroscopic appearances were quite unlike the condition. Causation by a hitherto unknown virus could not be proved, but the possibility remained until another microorganism was demonstrated. There was no histological trace of toxoplasmosis, pentastomiasis or any other parasitic condition.

No feature of the case is incompatible with the diagnosis of tuberculosis, but a few points require comment. The occasional impossibility of distinguishing between syphilis and tuberculosis without special staining has long been recognized. All types of histological appearance seen in this case, from the gumma-like nodule to the radial arrangement of the epithelioid cells around the necrotic tissue, are described in standard text-books. Even the accumulations of polymorphonuclear cells may be a reaction to the organism of tuberculosis just as well as to a secondary organism. The non-specific reactions in the duodenum and in the guinea-pig liver make one pause before a final diagnosis; but the experience is not new (McDonald and Weeds, 1950; Soltys and Jennings, 1950; Bretey, 1944), and the finding of appropriate organisms in the patient's tissues by two methods *plus* the development of inflammatory and allergic reactions in the guinea-pig injected first with the ascitic fluid and later with tuberculin and the presence of acid-fast and alcohol-fast organisms in the affected guinea-pig's liver all combine to substantiate the diagnosis of tuberculosis.

CASE II.—F.M., a girl, aged six years, was admitted to hospital in a poor general condition on January 9, 1925. Her father had "open" tuberculosis. She had a short, harsh cough, and had cramping abdominal pain. She was very

FIGURE XII.

Case III. Lung, showing fibrous nodule at lower left, and carcinomatous tissue mixed with chronic inflammatory tissue on the right (× 85).

thin and feverish. Enlarged, tender cervical lymph glands were present, and the spleen was readily palpable. Sputum examination revealed acid-fast and alcohol-fast organisms resembling *Mycobacterium tuberculosis*.

The fever continued and she became progressively weaker, complaining of difficult breathing and abdominal pain; she died on February 7, 1925.

Post mortem, widespread tuberculosis was found, involving lungs, meninges and abdominal viscera. Dr. J. V. Duhig supplied the specimens of liver and lung to the museum.

Multiple pale white rounded nodules were scattered through the fatty liver; their size varied about one centimetre in diameter. Examination of sections revealed central necrosis and peripheral granulomatous tissue, with many lymphocytes, a few plasma cells, an occasional giant cell, numbers of epithelioid cells and slight fibrosis (Figure XI). A few acid-fast and alcohol-fast organisms were found. The lung contained a number of similar nodules as well as the more usual irregular caseous tuberculosis.

The histological similarity of these rather well-established tuberculomata to some of the lesions in Case I is apparent.

CASE III.—E.Z., a male Filipino, aged fifty years, was admitted to the Brisbane Hospital on October 18, 1950, because of loss of power in the right arm for seven days, developing weakness in the right leg, and pain in the back. A fight had occurred at some indefinite date and he had fallen on the way to hospital. He evidenced considerable depression, which he attributed to his wife's desertion, and he was given therapeutically three electric shocks. But he remained morose, seldom speaking, and died on October 29, four days after electroplexy was stopped. Pyrexia occurred only on the last day.

Post-mortem examination revealed a recent large hæmorrhage in each cerebral hemisphere, and similar but smaller hæmorrhages in adjacent areas of the brain and cerebellum.

The apex of the right lung was shrunken, hard and irregular. It contained three nodules which appeared to have dense fibrotic walls and necrotic middles. The largest was about 1·2 centimetres in diameter and its walls were particularly hard. Around these hard nodules a little thin yellow pus was visible in the adjacent soft and darkly pigmented lung. Other lobes did not appear affected. The tracheo-bronchial lymph glands were enlarged, up to about 2·5 centimetres in diameter, and were very hard and white flecked with black.

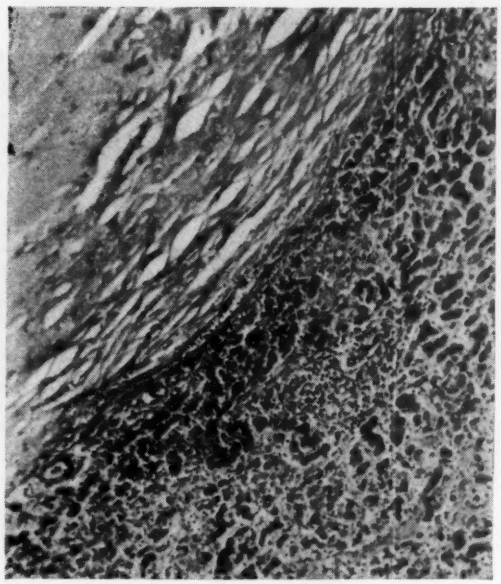

FIGURE XIII.

Case IV. Liver showing fibrous nodule with surrounding chronic inflammatory infiltrate (× 85).

In the right lobe of the liver were two rounded collections of thick, creamy yellow material, one just above the gall-bladder, one up near the bare area. The rest of the liver appeared normal.

Histological examination of sections of the lung suggested tuberculosis, and in one part carcinoma. The inflammatory lesion was partly irregular and active, but partly, in the nodules, rounded and densely fibrotic. Examination of the hardest nodule revealed fibrous tissue and carcinoma (Figure XII), and the lymph glands were enlarged by metastases. In the liver lesions were much central necrosis, peripheral fibrosis and chronic inflammatory infiltration (Figure X).

Numerous acid-fast and alcohol-fast organisms were found in direct smears from the right lung apex, a few in smears from the necrotic tissue in the liver.

The exact relation between the cerebral hæmorrhages and accident, therapy, or organic disease could not be determined. Bronchogenic carcinoma and pulmonary tuberculosis may be found together more frequently of late (Shefts and Hentel, 1950), but coexistence of the two is still uncommon, and no other relationship has been shown, so they are simply recorded here as coincidental. Even without cultural proof it is believed that the finding of the acid-fast and alcohol-fast organisms in smears from what is histologically similar to tuberculous tissue fairly well establishes the lesions as tuberculomata.

CASE IV.—R.C., a man, aged seventy-three years, was reported in good mental condition until an attack of giddiness, which was followed by slow cerebration. Four days later, on December 2, 1950, he was admitted to the Brisbane Hospital, but he was disorientated and his answers to questions trailed off into silence. Examination revealed slightly increased tendon reflexes on the right side and an equivocal right plantar response. His blood pressure was 150 millimetres of mercury, systolic, and 90 millimetres, diastolic. Some neck stiffness was noticed, but was thought voluntary. His temperature was normal and remained so. He became restless, then drowsy, and died on December 10.

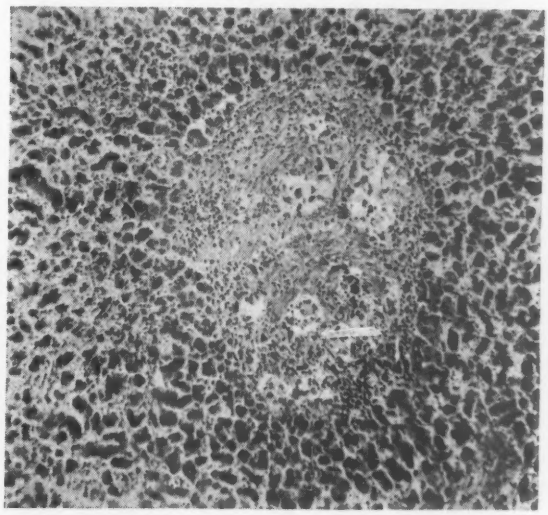

FIGURE XIV.

Case IV. Liver, showing epithelioid-cell tubercle which was immediately adjacent to the field in Figure XIII (× 85).

Post-mortem examination revealed a large collection of caseous material, about 7·0 centimetres long and about 2·5 centimetres in diameter, enclosed in firm fibrous tissue at the base of the left lung. Several smaller caseous foci and a few densely fibrotic parts were scattered through the left lung. In the right lung were many fibrotic nodules. Pleural adhesions covered both lungs.

In the white matter of the brain deep to the left parietal area was a small, round, greyish nodule about three millimetres in diameter. A few small, hard, white plaques were found on the leptomeninges, some separate, others clustered.

The right lobe of the liver contained two pale yellow nodules. The larger, about eight millimetres in diameter, projected slightly from the surface. The other, a little smaller, was partly calcified and situated deep in the liver tissue.

Right renal calculus, right hydronephrosis, slight left hydronephrosis, and a spongy, moderately enlarged prostate were other abnormalities found.

Histological examination of sections indicated fibro-caseous tuberculosis in the lungs, a tuberculoma in the brain (Figure XV), and small tubercles on the meninges. The non-calcified nodule in the liver was composed mainly of dense acellular fibrous tissue, and around the periphery was a thin layer of cellular fibrous tissue with a number of lymphocytes (Figure XIII). A little away from the edge of the main nodule, however, were at least three epithelioid-cell tubercles (Figure XIV). A few acid-fast and alcohol-fast organisms were found. The portal tracts were surrounded by increased fibrous tissue and numerous lymphocytes. The other nodule

in the liver was composed of fibrous tissue with central calcification (Figure XVI), but no epithelioid-cell tubercles were evident.

Though bacteriological proof is again lacking, the appearances of lesions in the lung, brain, meninges and liver, with the presence of appropriate organisms, though few, point to a diagnosis of tuberculosis and tuberculomata.

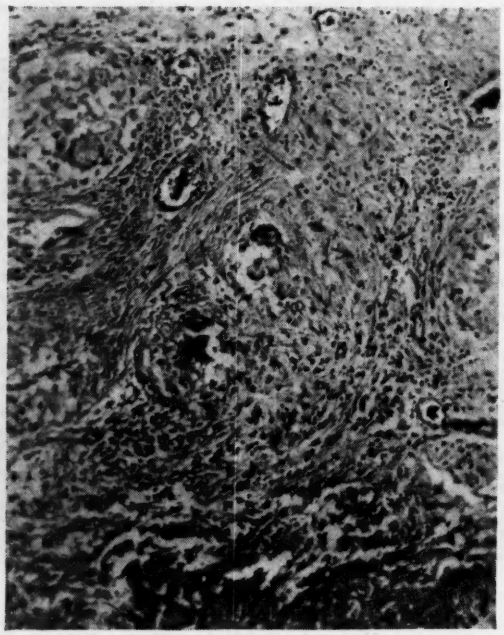

FIGURE XV.

Case IV. Brain, showing edge of tuberculoma, with caseation necrosis at the bottom (× 85).

CASE V.—T.G., an aboriginal woman, mother of three children, was admitted to the Brisbane Hospital in 1936, when aged twenty-nine years, suffering from peritonitis and right basal pneumonia and pleurisy. At operation both uterine tubes were found inflamed, with fibrin on the surface, and pus was free in the pelvis. Both inflamed tubes and the normal-looking appendix were removed.

She was next admitted to hospital on January 21, 1950, aged forty-three years, because of pain in the region of the left costal margin following a fall. An enlarged liver was felt four fingers' breadth below the right costal margin, but no cause was discovered. The blood reacted to the Wassermann test (++), to the Kahn test (+), and to the Eagle test; but on repetition four days later the result was negative, and eight months later it was again negative. The cephalin-cholesterol flocculation test produced a positive reaction (++) in forty-eight hours. The blood pressure was 240 millimetres of mercury, systolic, and 130 millimetres, diastolic. She vomited and had some abdominal pain in hospital, but no definite diagnosis was made. On February 11 she was allowed to go home, in the belief that she was suffering from cirrhosis or malignant disease of the liver.

Her final admission to hospital was on October 6, 1950, after she had felt ill for about a year. She had had no menstrual periods, had suffered attacks of vomiting, and had noticed enlargement of her abdomen. Dyspnœa was felt on exertion, and then even at rest. She had a cough, but no chest pain. Her second child had died of "a weak chest", but the date is not recorded.

Signs of right basal pneumonia with effusion were found as well as the enlarged liver and hypertension, the systolic blood pressure being 180 millimetres of mercury and the diastolic pressure 110 millimetres. Her temperature persisted between 102° and 104° F. for nine days in spite of penicillin and sulphamerazine therapy. Digitalis and mersalyl were also administered. An electrocardiogram on October 13, 1950, showed the *P-R* interval to be 0·22 second. The blood urea and serum protein contents were normal. Streptomycin was given from October 14, and in the next three days the temperature fell to normal. *Paracentesis thoracis* on October 17 yielded 350 millilitres of dark amber fluid. Next evening, soon after a meal, the patient was found dead in bed.

Autopsy showed the subject to be an aboriginal woman, five feet four inches in height. Her heart weighed 410 grammes and was contracted and empty. The myocardium was hypertrophied, but the valves were normal. Coronary atheroma was slight in degree. The pulmonary arteries were normal.

The pleura over the lower lobe of the right lung and over the diaphragm was very thickened and very hard, white except for a few tiny yellow foci. The lower lobe was collapsed and the pleural space was occupied by about 600 millilitres of clear yellow fluid, but the middle lobe of the right lung was firmly adherent to the chest wall, and the pleura over the upper lobe of the right lung was only slightly thickened and streaked with fibrinopurulent exudate. The left pleural cavity contained only a little clear fluid. The lungs otherwise appeared normal. Myriads of tiny white nodules, varying in diameter up to two millimetres, were scattered over the peritoneum.

The liver was pale and rather coarsely nodular, with fibrous tissue breaking the cut surface into yellowish-brown nodules up to eight millimetres in diameter. The gall-bladder was normal.

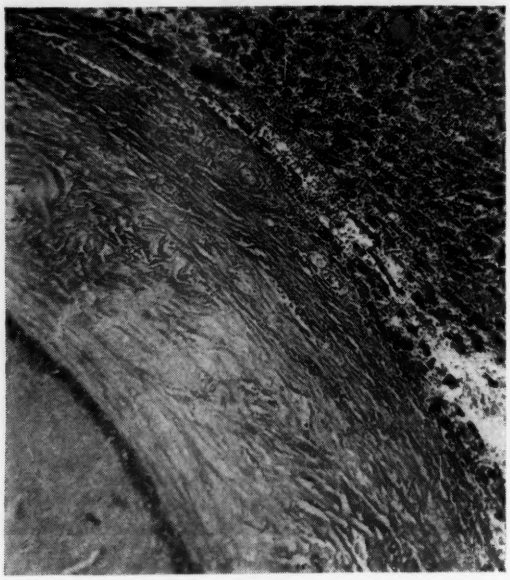

FIGURE XVI.

Case IV. Liver, the nodule showing central calcification (× 85).

Three very small, hard, white nodules were found close together in the upper outer quadrant of the left breast, about two centimetres from the nipple. No enlarged regional lymph glands were found. A small black nodule, about five millimetres in diameter and three millimetres thick, was found in the middle of the left adrenal gland. The kidneys weighed about 190 grammes each and appeared normal.

Histological examination of sections of the pleura revealed fibro-caseous tuberculosis lesions, mainly fibrous tissue, and the peritoneal nodules were typical tubercles (Figure XVII). Fibrous tissue tracts passed irregularly throughout the liver, through lobules as well as round them. Only two typical epithelioid-cell tubercles with giant cells were seen deep in the liver, but there were a number of atypical or rudimentary tubercles (Figure XVIII), and the fibrous tissue with numerous associated lymphocytes was continuous with similar tissue round the numerous typical tubercles at the surface. Six acid-fast and alcohol-fast organisms were

found deep in the liver in one section, and a number were found in smears from the pleural effusion and ascitic fluid.

Intraductal carcinoma of the breast was present in the small nodules described. Myocardial hypertrophy was the only recognized abnormality in the heart. Examination of the kidneys revealed benign nephrosclerosis. The black nodule in the left adrenal was in the inner cortex and consisted of cortical cells containing large numbers of granules with a staining reaction to Giemsa and the routine stains similar to melanin.

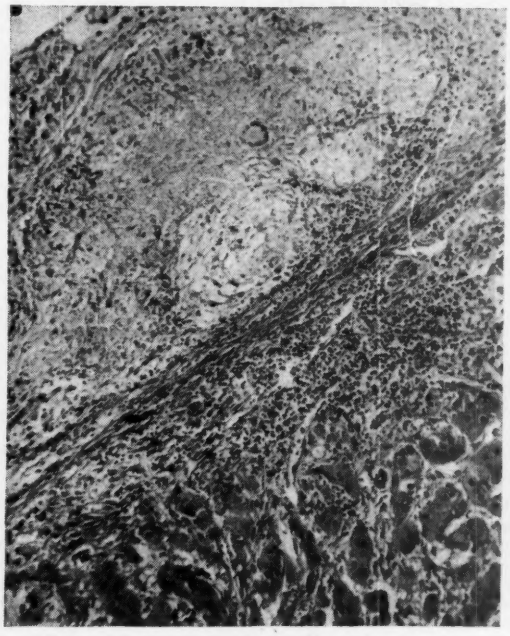

FIGURE XVII.
Case V. Liver, with peritoneal tubercle on the surface (× 85).

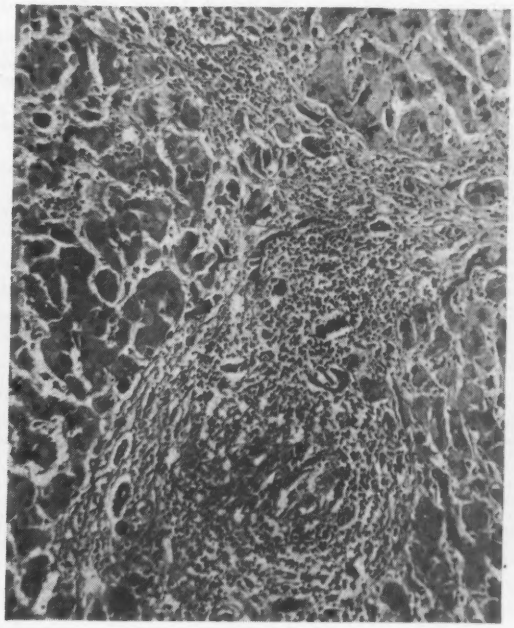

FIGURE XVIII.
Case V. Showing tubercle, which is situated deep in the liver (× 85).

The histological similarity to diffuse syphilitic cirrhosis is pronounced, but serological test results are against the diagnosis, and clinical and pathological evidence makes tuberculosis reasonably certain. The possibility of syphilis, with a negative response to the complement-fixation test, coexisting with tuberculosis may be considered; but without better evidence the possibility remains remote. There also exists the possibility of tuberculosis complicating or being complicated by portal cirrhosis of nutritional or other cause. Patek (1947) records tuberculosis as a complication of portal cirrhosis as being still found in 2% or 3% of autopsy cases, and adds that it used to be more frequent. In the present case, although it looks as if the fibrosis around the tubercles in the liver resulted from invasion by the organism, the appearance may be misleading. But it would still be prudent to stop before accepting the implication by some writers that tuberculosis is always a complication and does never itself produce fibrosis throughout the liver.

Carcinoma of the breast appeared unrelated to other findings. Increased black pigment in the adrenal cortex would seem most probably associated with the aboriginal race, although it has not been noticed in a few other post-mortem examinations on aborigines. No cause of hypertension was apparent. Excess cortical hormone administration does lead to hypertension (Hartman and Brownell, 1949), and a damaged liver might interfere with inactivation; but as far as is known there is no relation between such a pigmented cortical adenoma and hypertension.

Whether death was due to toxins resulting from tuberculosis, or from failure of the liver to detoxify digitalis, or from insufficient blood supply to the hypertensive heart, or from some other cause or combination of causes can only be the subject of speculation. What is now clear is that the primary cause of the patient's severe illness was tuberculosis.

Summary.

Tuberculosis of the liver, a relatively rare condition, is briefly reviewed.

For correct diagnosis of tuberculosis the importance is stressed of supplementary histological and bacteriological investigations. Reasons are indicated.

Five cases are reported of tuberculosis involving the liver; four of the subjects had tuberculomata and one had chronic disseminated tuberculosis and cirrhosis. Other parts affected by tuberculosis include lungs, pleura, peritoneum, duodenum, brain, meninges, spleen, lymph glands, and skin. Associated conditions with no apparent relation to tuberculosis include hæmochromatosis, carcinoma of the lung, carcinoma of the breast, and a small, black, pigmented adrenal cortical adenoma.

Interesting clinical points are to be found in the case reports, but after post-mortem findings are described several features of pathological interest are selected for comment or brief discussion.

Acknowledgement.

Grateful acknowledgement is made of help received from many different persons in many different ways, far too numerous to list in detail, in the gathering and preparation of this material.

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INTRAVENOUS THERAPY IN SURGERY: A REVIEW.

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Sydney.

DURING the last two decades the advances made in the maintenance of a normal internal environment in the face of a variety of pathological conditions have led to a saving of life which is comparable to that resulting from the development of the various antibiotics now available.

A clearer understanding of the biochemical and physiological principles involved, the standardization and simplification of methods of administration, and the ready availability of a variety of substances for intravenous use have placed a powerful weapon in our hands. But it is a two-edged sword that we grasp, to be used with care and discrimination and with a clear understanding in each individual case of precisely what we propose to achieve. There is no place for rule-of-thumb methods when fluid, mineral and protein requirements are being calculated. They can be estimated mathematically in nearly every case with comparative simplicity. There is no room for empiricism and no necessity for it. Black has pointed out that advances in intravenous technique have made it possible to drown a patient, or pickle him, in a very short space of time, and one or other of these misfortunes or the equally unpleasant alternative of uncorrected dehydration will occur only too often unless a few basic principles are borne in mind and correctly applied.

BIOCHEMICAL AND PHYSIOLOGICAL ASPECTS.

The fluid content of the body is disposed in three compartments, each of which is separated from the other by a selectively semipermeable membrane, so that the contents of each compartment, although distinct, are mutually interdependent, and changes in any one are rapidly reflected in the others, since all three compartments must remain in osmotic equilibrium (Figure I).

The first compartment contains the intracellular fluid. This is composed of potassium and magnesium balanced by phosphate and protein with smaller amounts of bicarbonate and sulphate. The second compartment contains the tissue fluid, composed largely of sodium on the one hand and chloride and bicarbonate on the other. Finally, there is the circulating plasma, similar in composition to the tissue fluid except that it contains an appreciable amount of protein (Figure II).

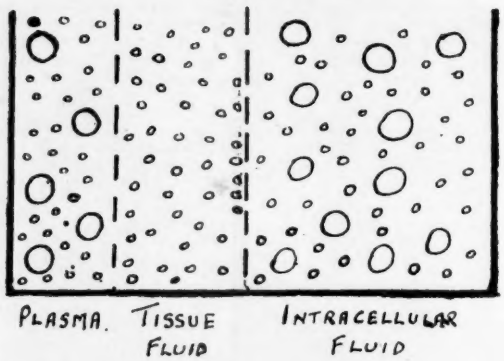

FIGURE I.
Showing the osmotic relationship between the body fluid compartments. (After Marriott.)

In addition to osmotic equilibrium it is necessary for the various compartments to remain in electrolytic equilibrium, both internally and in relation to one another. The most efficient method that the body has at its disposal for the maintenance of the normal pH of the intracellular and extracellular fluids is the adjustment of the carbon dioxide : bicarbonate ratio by the sensitivity of the respiratory centre (which allows the lungs to blow off carbon dioxide when the plasma bicarbonate level is reduced) and by the chloride shift mechanism.

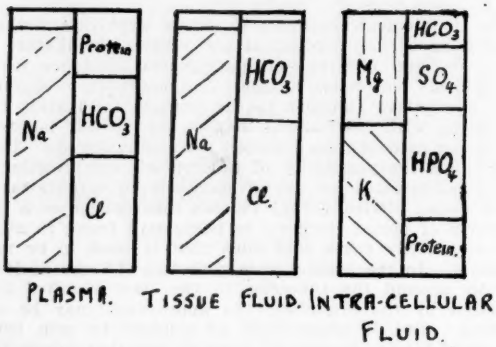

FIGURE II.
Showing the composition of plasma and tissue fluid (extracellular) compared with that of intracellular fluid. (Simplified from Coller and Maddock.)

The third factor which must receive consideration is the volume of circulating blood. Should this fall for any reason the venous return is lessened, the stroke volume is reduced, and eventually a point is reached beyond which the carotico-aortic reflexes can no longer satisfactorily maintain the blood pressure. The effects of tissue anoxia then begin to become manifest, and unless the blood volume is restored promptly the condition becomes irreversible, since any fluid introduced at this stage will pool in the dilated and unresponsive capillary bed.

Four factors therefore demand consideration in any case in which it is proposed to introduce fluid intravenously. These factors are as follows: (i) The restoration and maintenance of an adequate circulating blood volume and the avoidance of overloading the circulation with an excessive amount of fluid. (ii) The correction of any electrolyte imbalance. In effect this means estimating the amount of sodium, potassium and chloride required by the patient. (iii) The supply of those substances required by the body to maintain osmotic equilibrium, that is, water, salt and protein. (iv) The correction of anæmia and supply of carbohydrate in the form of glucose.

With these four factors in mind it is necessary only to have a clear picture of the changes brought about by various pathological conditions and of the methods by which these changes can be detected, to put their correction on a rational basis.

Pathological Changes.

The various pathological changes which may require correction by intravenous therapy will now be considered individually.

Water Loss.

Pure water deficiency is uncommon but does occur. Apart from actual starvation, it can occur in head injuries associated with prolonged unconsciousness, when fluid replacement is lacking or inadequate, and in debilitated patients who, because of weakness or inanition, fail to make their needs known.

The body requires some 2600 millilitres of water a day to replace losses in evaporation and urinary excretion (Table I).

TABLE I.

Water Lost by the Body Daily (Marriott).

Means of Water Loss.	Volume. (Millilitres.)	
Lungs	400	
Skin (insensible perspiration)	600	
Total water lost by vaporization	—	1000
Urine		1500
Fæces		100
Total water lost		2600

Coller and Maddock put daily water requirements at 2000 to 2500 millilitres under normal conditions. For a patient who is feverish, sweating or under hot conditions these figures are raised to 3000 to 3500 millilitres per day.

The urinary excretion of water consists of a minimum volume required for the excretion of waste products and the surplus water ingested by the body. The former of these amounts varies, depending on the concentrating power of the kidney and the actual amount of waste material required to be excreted. If we take an average daily excretion of 35 grammes of waste end-products of metabolism, the variation in the minimum volume required for its clearance can be seen from the accompanying diagram (Figure III).

The ability of the kidneys to concentrate the urine to the normal maximum adult level of 1030 or more is diminished in infancy and old age. Local renal conditions, such as acute and chronic nephritis and obstructive renal disease, also result in defective concentrating power. It is not generally realized that the efficiency of the kidney is also much impaired after any episode of severe or prolonged dehydration, and during and after secondary shock.

In addition, there is an increase in the total amount of waste products which will require to be cleared in infancy and childhood (owing to the higher rate of metabolism) and in any condition in which the basal metabolic rate is raised, such as any febrile disturbance and thyreotoxicosis. Waste products are also increased in dehydration and very much so after any hæmorrhage into the gastro-intestinal tract (Black).

The effect of pure water depletion on the extracellular and intracellular compartments is to produce a generalized concentration, which is, however, greater in the intracellular compartment, as water tends to be given up by the cells to maintain the circulating blood volume (Figure IV).

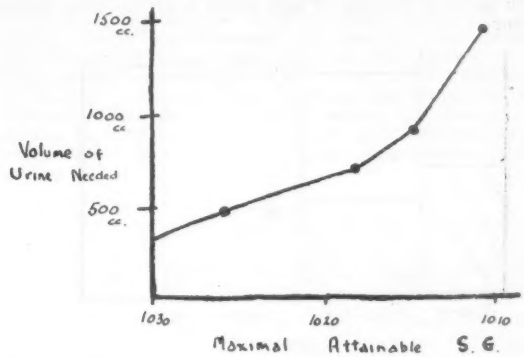

FIGURE III.

Showing the volume of urine needed to excrete 35 grammes of waste daily at various maximal attainable specific gravities. (From Marriott.)

Salt Loss.

Salt loss is seen in such conditions as intestinal obstruction, repeated vomiting from any source or diarrhœa, especially in infants, when the fluid lost is replaced by water alone without the addition of sodium chloride.

Fluid lost from the upper part of the gastro-intestinal tract by vomiting or suction contains an excess of chloride over sodium, while with diarrhœa the reverse is the case (Coller and Maddock). Sodium loss is less easily compensated than chloride loss, since chloride loss can be replaced to a considerable extent by bicarbonate, so that the electrolytic balance is maintained.

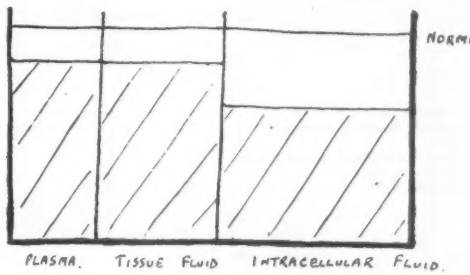

FIGURE IV.

Showing the effects of pure water loss. (From Marriott.)

It is interesting at this stage to note the sodium chloride content of various body fluids which may have to be replaced (Table II).

Thus it can be seen that the sodium chloride content of fluid lost from the body averages around five grammes per litre. If sodium is lost in excess of chloride the carbon dioxide-combining power of the blood will be lowered, and when chloride loss is in excess the reverse holds.

In pure salt depletion the effect on the intracellular and extracellular compartments is vastly different from that which occurs in water loss (Figure V).

It can be clearly seen that the effects of salt loss are of a much more serious nature than simple water loss. The brunt of the fluid loss falls on the extracellular compartment, since the kidneys excrete water in an effort to maintain osmotic equilibrium. The intracellular compartment is not depleted, indeed water may pass from the tissue

spaces to the cells. Thus the circulating blood volume may be seriously depleted, leading to a shock-like condition which further diminishes the circulating fluid volume, and so a vicious circle is established.

A mixed water and salt loss is a more common occurrence than either pure water or pure salt deficiency, but, even so, it is the loss of salt which is of the more serious import.

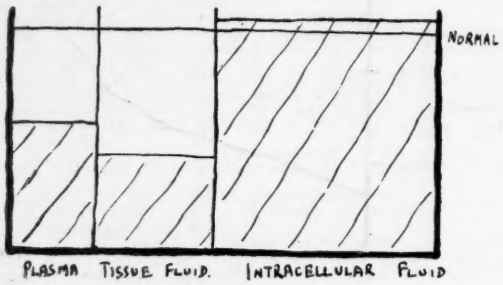

FIGURE V.

Showing the effects of pure salt loss. (From Marriott.)

Salt excess, on the other hand, such as may occur from the over-enthusiastic infusion of large amounts of normal saline, results in the pooling of fluid in the tissue spaces with the production of œdema. This is of most serious consequence in the lungs, and many patients developed pulmonary œdema, not infrequently with fatal results, in the early days of intravenous therapy before the serious effect of excessive salt administration were fully understood.

TABLE II.

Average Sodium Chloride Content of Various Body Fluids. (From Coller and Maddock.)

Body Fluid.	Average Sodium Chloride Content. (Grammes per Litre.)
Vomitus	3·3
Gastro-duodenal drainage	5·7
Bile	5·1
Fluid from small bowel fistula	5·2
Diarrhœa stool	4·3
Normal saline	8·5

Potassium Loss.

It has only recently been realized that potassium loss occurs in a variety of pathological conditions and may have serious consequences. Hypopotassæmia results in definite electrocardiographic changes and reversible and usually non-fatal muscular paralysis. It may be associated with a low intracellular potassium level, which may well jeopardize recovery in serious cases (Danowski).

Bellet and Nadler *et alii* have shown that there is a pronounced potassium loss after all major operations, regardless of their nature. In particular, the fluid lost in intestinal obstruction, either by vomiting or by aspiration, contains relatively large amounts of potassium, up to five times the concentration present in the serum. There is also a pronounced loss of potassium in states of dehydration, particularly in the presence of alkalosis. The loss of nitrogen from the cells which occurs post-operatively or during any severe illness also results in potassium loss.

It is suggested therefore that, when intravenous therapy is considered necessary, Ringer's solution be used in lieu of normal saline to correct both sodium chloride and potassium loss. This contains 0·9 gramme of sodium chloride, 0·03 gramme of potassium chloride, and 0·025 gramme of calcium chloride in each 100 millilitres. This is the proportion in which these substances are present in plasma.

Protein Loss.

The healthy adult requires protein to replace the loss of tissue protein which takes place from ordinary "wear and tear". When receiving a nitrogen-free diet he will excrete around three grammes of nitrogen daily derived from his own protoplasm and equivalent to 18·75 grammes of tissue protein. In order that the body shall obtain a sufficient quantity of suitable amino-acids to maintain its own protoplasm and manufacture various secretions and essential material, nitrogen equilibrium can be established only if all the "essential" amino-acids are available in adequate amounts. Those not required are broken down and discarded. It has been found that nitrogen equilibrium can be established on a protein intake around 40 grammes per day. However, the true protein requirement over an extended period of time appears to be somewhat more than one gramme per kilogram of body weight or 70 to 100 grammes per day (Best and Taylor).

Growing children require, in proportion, considerably more protein. Up to one year they need about four grammes per kilogram of body weight, and this falls gradually until the sixth year when it amounts to about 2·6 grammes per kilogram. This figure is maintained during the growth period.

In many pathological conditions the body's protein requirements are grossly increased. From 150 to 500 grammes of protein or more may be required daily to maintain nitrogen equilibrium, and in most cases it is impossible to supply even this lower figure by normal means.

When the body is in negative nitrogen balance, as it is during most severe illnesses or after operations, it first uses up the protein reserves distributed throughout the body. Only then does a breakdown of tissue protein occur. When this does take place the plasma protein level commences to fall, for there is a dynamic equilibrium existing between plasma and tissue protein.

The metabolism of protein depends on good liver function, and assessment of hepatic sufficiency is becoming more and more important in major surgery.

Hypoproteinæmia may be due to a variety of causes, and not infrequently several of these are acting in combination. They may be grouped as follows: (i) Pre-hepatic causes—inadequate nutrition, digestion or absorption. (ii) Hepatic causes—depressed liver function. It must be realized that hypoproteinæmia in itself will depress liver function and make it more vulnerable to other noxious influences. (iii) Post-hepatic causes—severe or prolonged diarrhœa, pronounced albuminuria, hæmorrhage or serum loss (burns, pleural or peritoneal effusions or transudates).

Nutritional œdema, due to interference with osmotic equilibrium, will appear when the plasma protein level is reduced below 5·5 grammes per 100 millilitres (or more particularly when the serum albumin level falls below 3·3 grammes *per centum*).

In post-operative hypoproteinæmia several factors are operating. The pathological condition requiring operation may have reduced protein intake for some time (for example, gastro-intestinal carcinoma) or caused excessive protein loss (for example, diarrhœa, albuminuria).

Pre-operative and operative hæmorrhage or serum loss and pre-existing liver insufficiency also react adversely. Anæsthesia, major surgical procedures and operative handling of the tissues all increase protein breakdown. There may have been a pre-operative period when the protein intake was grossly deficient. Shock, fever, vomiting and tissue injury may all add to the loss of protein by the body. As would be expected, it is found that the major part of this loss takes place in the first five days after operation, when food intake is generally limited.

Calorie and Vitamin Requirements.

The basal heat production of the human body is approximately a Calorie per kilogram per hour, and in order that the tissues shall not be consumed for fuel the caloric value of the ingested food must balance the heat eliminated by the individual during the same period. Thus, even under basal conditions, the average person

requires more than 1600 Calories per day. When the metabolic rate is increased (as it is by fever or in the post-operative period) the requirements are considerably higher.

When a patient is being maintained solely by the intravenous route his caloric intake is usually grossly inadequate (see Table III). This is of little consequence if adequate oral feeding can be rapidly resumed, but when this is not possible, then the caloric content of the fluid administered intravenously must be increased to adequate proportions to guard against tissue destruction, depletion of the body's reserves of carbohydrate and fat, incomplete oxidation of fats with the appearance of ketone bodies, and the inefficient utilization of protein in the absence of sufficient carbohydrate.

TABLE III.

Type of Fluid.	Volume. (Millilitres.)	Calories. (Approximately.)
Whole blood or serum ..	100	30
"Casydrol"	100	40
5% glucose solution ..	100	20
10% glucose solution ..	100	40

Vitamin requirements in conjunction with parenteral therapy require consideration only in exceptional cases, since, in the majority of instances, oral administration can be resumed before parenteral replacement is necessary. However, should vitamin therapy be considered necessary in any particular instance, when oral administration is not practicable, then one of the numerous suitable preparations now available may be administered parenterally.

BASIC REQUIREMENTS.

It is now possible to estimate the basal daily requirements of a patient who must be maintained for any length of time by the intravenous route (Table IV).

TABLE IV.

Basic Daily Requirements.

Item.	Basal Daily Requirement.
Fluid	2500–3000 millilitres.
Sodium chloride (potassium and calcium in proportion) ..	5 grammes.
Protein	70 grammes.
Energy requirements	1500 Calories.

So long as a daily urinary output of 1500 millilitres is provided for and maintained, the finer adjustment of the various electrolytes may be safely left to the kidneys. It is necessary only to provide potassium and calcium in the proportions in which they are present in the plasma (as is done in Ringer's solution) and the kidneys will retain or excrete them as is necessary to adjust the electrolyte balance in blood and tissues. This regulatory power of the kidney will fail only if the urinary output is allowed to fall. Even in the presence of a fairly high degree of impairment of renal function, the blood chemistry can be maintained within normal limits if the daily urinary volume can be kept at or above 1500 millilitres.

The basal daily requirements are met fairly closely by a litre of serum and two litres of 10% glucose in distilled water (Table V).

As serum is often in short supply the following alternative combination may be used (Table VI). It is deficient in protein but otherwise fairly adequate.

REPLACEMENT THERAPY.

Restoration of Water and Salt Balance.

A patient clinically presenting manifest evidence of dehydration can be presumed to have lost 6% of his body weight (Coller and Maddock, 1940). His fluid needs for the succeeding twenty-four hours can be estimated as basic requirements (3000 millilitres) *plus* at least 4000 millilitres to compensate for his dehydration. It has been noted previously that fluid loss by the body averages about five grammes of sodium chloride per litre, so that a dehydrated patient requires 20 grammes of sodium chloride (and other electrolytes in proportion) above his basic needs. These requirements are met by two litres of Ringer's solution and two litres of 10% glucose in distilled water. In addition any further fluid losses must be promptly replaced. Whether from aspiration, vomiting, diarrhœa, intestinal or biliary fistula, the amount lost should be measured or estimated as accurately as possible every twelve hours and a corresponding volume of fluid

TABLE V.

Substance Administered.	Quantity. (Millilitres.)	Caloric Value.	Protein Content. (Grammes.)	Sodium Chloride Content. (Grammes.)
Serum	1000	300	70	6
10% glucose in distilled water ..	2000	800	—	—
Total	3000	1100	70	6

added to the daily requirements, half as Ringer's solution and half as 10% glucose in distilled water.

It is doubtful whether more elaborate methods of replacement, requiring repeated laboratory investigations, are worth while. Coller and Maddock recommend giving 0·5 milligramme of salt per kilogram of body weight for every 100 milligrammes that the plasma chloride level is below the normal value of 560 milligrammes *per centum* (expressed as sodium chloride). However, they themselves found that this approximated very closely in

TABLE VI.

Substance Administered.	Quantity. (Millilitres.)	Caloric Value.	Protein Content.	Sodium Chloride Content. (Grammes.)
Ringer's solution	500	—	—	4·5
10% glucose in distilled water ..	2500	1000	—	—
Total	3000	1000	—	4·5

dehydrated patients to the amount indicated by the above simple method.

The Fantus test, as a ward procedure, is of some value in providing a rough estimate of urinary chloride excretion.

Protein Replacement.

Where possible protein requirements should be met by oral administration. When this is not possible, or intake is inadequate, recourse must be had to the intravenous route. In most surgical cases no particular protein replacement is needed since the patient replaces protein when normal diet is resumed. However, it should always be borne in mind, particularly when protein intake has been deficient or utilization excessive or inadequate for some time pre-operatively, and when some time is expected to elapse after operation before adequate amounts of protein can be taken by mouth. In such cases every effort should be made to keep the normal protein intake as high as possible; even then the patient will probably still be in negative nitrogen balance for some time.

Oral Administration of Protein.

Protein may be administered by mouth in amounts up to 150 grammes, depending on how much the patient will tolerate and on the condition under treatment.

It may be given by oral tube in amounts up to 90 grammes. However, this method is likely to cause troublesome distension and diarrhœa and is not, in general, recommended.

Orally Administered Amino-Acids.—It is felt that the value of orally administered amino-acids is limited. Once again the tolerance of the patient is the limiting factor, and it is felt that they offer little advantage, either in ease of administration of rapidity of absorption, over whole protein.

Intravenous Administration of Blood and Serum.

If large amounts of protein are required in a short space of time the intravenous route should be used. It obviates any risk of further protein depletion from vomiting and diarrhœa, it is rapid and accurate, and utilization is maximal. Blood is used when anæmia is an additional factor, but when one is dealing solely with protein-lack then serum is preferable.

It takes 375 grammes of protein given daily for ten days to raise the serum protein level from five to seven grammes *per centum* (Willinsky, 1945). Therefore, it is scarcely possible to administer excessive protein in these cases. Basal and fluid replacement requirements should be estimated and as much as possible of these given as serum, depending on the availability of this commodity.

There appears to be no particular advantage in administering plasma in concentrated form (10% to 12% protein).

Amino-Acid Preparations.

It is considered that amino-acid preparations have only a limited field of usefulness in surgical cases. Even with modern preparations, febrile reactions and phlebitis are not infrequent. However, when the need for parenteral protein replacement extends over an appreciable length of time, the use of these preparations results in a saving of plasma and the supply of all essential amino-acids in a readily utilizable form. Each litre of solution contains 60 grammes of protein as amino-acids; 30 drops per minute is the maximum rate at which it is advisable that they should be administered.

Human Transudate Fluid.

Human transudate fluid has a protein content of from 1% to 7% and has been used as a source of available protein in a variety of conditions. However, it is not considered that this method has much to recommend it.

Restoration of the Circulating Blood Volume in Secondary Shock.

The condition of secondary shock develops when the venous return is diminished owing to blood or serum loss; this loss may be external, internal or interstitial—that is, into the tissues themselves. This results in a fall of blood pressure, which, if not compensated by physiological mechanisms or by the introduction of additional fluid into the circulation, will go on to produce tissue anoxia and further depletion in the venous return until a point is reached at which the condition becomes irreversible. Intravenous therapy must, therefore, be instituted promptly in these cases in order to forestall the pernicious effects of tissue anoxia.

When shock is due to blood loss, blood should be used as the replacement fluid; in shock due to extensive burns, serum is to be preferred. Saline has no place in the treatment of secondary shock, since it leaves the circulation as rapidly as it is introduced and, if given in appreciable quantities, may bring about pulmonary œdema. Amino-acid preparations are, of course, of no use in the treatment of shock, since they are taken up by the cells and do not remain in the circulation to exert an osmotic effect.

The rate of transfusion is dependent more upon clinical judgement than upon laboratory methods. Blood (or serum) should be given through a cannula as rapidly as possible at first. Positive pressure may be used or more than one vein may be employed. A cannula is preferred to a needle, since blood may be introduced through it more rapidly and there is less likelihood of its blocking or coming out of the vein at a critical moment.

A rapid rate is maintained until the systolic blood pressure is raised above 100 millimetres of mercury, when it is slowed to 60 drops per minute. Further transfusion depends on regular frequent observation of the blood pressure and pulse rate and serial estimations of the hæmoglobin value.

If the resources of a fully equipped pathological laboratory are available, it is an advantage to carry out serial estimations of the blood and serum specific gravity by the copper sulphate falling drop method every four hours. The hæmoglobin, hæmatocrit and serum protein values can then be charted. A rising hæmoglobin and hæmatocrit value in conjunction with a falling serum protein level is an indication that the rate of transfusion must be increased, as fluid is still being lost from the circulation. Conversely, as these figures approach one another, it indicates that the condition of shock is being controlled and that the rate of transfusion may safely be reduced.

Conclusion.

Thus it is possible, by appreciating the physiological principles underlying the maintenance of the normal fluid balance between the blood and the tissues, to assess with reasonable accuracy the requirements of the individual in various pathological conditions.

Various authorities have, from time to time, put forward methods by which it is possible to determine very precisely the deviations from normal biochemistry which occur and the manner in which they may be rectified. However, many of these are practicable only in experimental institutions and require close personal supervision. It is felt that the methods outlined here can be put into operation without imposing undue strain on the nursing staff, the pathology department or the surgeon himself.

Summary.

The biochemical and physiological aspects of normal fluid balance are reviewed.

The alterations that take place in extracellular and intracellular fluid and electrolyte balance and osmotic equilibrium in various pathological conditions are outlined.

The basic requirements of fluid, salt and protein are set down.

The method of restoring water and salt balance and replacing protein loss is discussed.

The role of intravenous therapy in the treatment of secondary shock is briefly reviewed.

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DICOUMAROL IN THE TREATMENT OF CORONARY OCCLUSION.[1]

By R. WHISHAW,
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MANY favourable reports of the treatment of coronary occlusion with anticoagulants have been published during the past four years. A recent article by Elliott Bresnick *et alii* (1950) is much less favourable, and many experienced physicians consider that this treatment should be reserved for special cases.

Because of these doubts, I decided to attempt an assessment of our results at the Royal Hobart Hospital in order to obtain some guidance for the future management of patients with coronary occlusion.

Dicoumarol Therapy.

It was not until January, 1949, that dicoumarol treatment was seriously begun at the hospital. In addition to the usual routine treatment, the drug was given for a period of four weeks, the dosage being regulated according to the prothrombin index. Owing to the wide variation of individual response, no standard dosage could be employed, and it was found to be difficult and sometimes impossible to keep the prothrombin index in the region of 25%, the ideal figure. Whether or not this is important is undecided, and in the present small group of patients no conclusion on this point could be drawn.

Table I indicates the degree of prothrombin control achieved in the six patients who died during or after treatment with dicoumarol. Heparin was not used in this series. A study of the prothrombin indices confirmed the fact that in some persons the action of dicoumarol was prolonged for a week or more after it had been discontinued.

Hæmorrhage.

There were five instances of mild to moderate hæmorrhage among the "treated" patients. The sites of bleeding were as follows: renal tract (three cases), lungs (one case), nose (one case). These patients recovered and gave no real concern. Vitamin *K* was given, but blood transfusions were unnecessary. The prothrombin index was not always unduly low when hæmorrhage occurred, and there were several very low readings among patients who had no hæmorrhage.

Material.

All patients admitted to hospital with coronary occlusion were not given dicoumarol, the decision being made by the physician in charge of the case.

As no "control" patients were used at the time, and as this paper deals primarily with an evaluation of the results of dicoumarol treatment, it has been necessary to use as "controls" those patients admitted to hospital during 1949 and 1950 who were treated on orthodox lines, together with some patients admitted to hospital during 1948 before this drug was used.

The possible fallacies in comparing "treated" patients with "controls", even when such a study has been preconceived, are emphasized in an excellent article by Tulloch and Gilchrist (1950) on this present topic, and also in a leading article in the same number of the *British Medical Journal.*

I have therefore been at pains to detail the necessary data for the "controls" to fulfil all requirements, so far as this is possible.

All available records of patients admitted to hospital with coronary occlusion (about 250) during the last three years have been examined. Unfortunately half of these had to be excluded because of insufficient information, doubt about the diagnosis, or death of the patients within twenty-four hours of their admission to hospital. The remaining records, which were otherwise unselected, were disappointingly small in number, only 125 being suitable for analysis, and producing 68 "treated" patients and 57 "controls".

[1] Read at a meeting of the Tasmanian Fellows and Members of The Royal Australasian College of Physicians, Hobart, March 17, 1951.

TABLE I.

Deaths During or After Dicoumarol Therapy.

Patient's Sex and Age (Years).	Duration of Illness.	Prothrombin Control.
Female, 69	6 weeks.	Good.
Female, 72	4 days.	Good.
Male, 69	11 days.	Good.
Male, 70	6 days.	Good.
Female, 58	10 weeks.	Fair.
Male, 38	9 days.	Poor.
Male, 64	6 weeks.	Poor.
Male, 61	4 weeks.	Poor.

In accordance with the method of Tulloch and Gilchrist (1950), these two groups of cases have been analysed in respect of age, sex, preexisting cardio-vascular disease, including previous attacks of coronary occlusion, duration from onset of symptoms to admission to hospital, presence of shock, thrombo-embolic episodes, and mortality rate up to four to six weeks after the attack, or discharge from hospital.

Comparison of the Two Groups.

Table II details the age and sex incidence of 125 cases of coronary occlusion—68 "treated" patients and 57 "controls". It will be seen that the highest incidence falls between the ages of fifty and sixty-five years, and that the two groups are comparable in regard to sex and age. The proportion of males to females is 3·5:1·0.

TABLE II.

Age and Sex Incidence in 125 Cases of Coronary Occlusion; 68 "Treated" Patients, 57 Controls.

Age. (Years.)	Males.		Females.	
	Controls.	Treated.	Controls.	Treated.
35	0	1	0	0
40	1	2	0	0
45	1	4	2	0
50	8	10	0	3
55	5	11	1	2
60	7	9	4	4
65	11	5	2	5
70	6	8	1	1
75	4	2	3	0
80	1	1	0	0
Totals ..	44	53	13	15

Preexisting Heart Disease.

The higher the proportion of patients with preexisting heart damage, the poorer will be the prognosis of the group; hence the necessity for comparing these factors.

Table III indicates that the numbers of patients suffering from preexisting angina of effort, congestive cardiac failure and previous attacks of coronary occlusion were fairly evenly distributed.

When both groups are included, angina had been present before the occlusion in 31% of cases, congestive failure in 8%, and in 15% previous myocardial infarcts had occurred.

Duration of Attack in Relation to Day of Admission to Hospital.

Another important factor which affects prognosis is duration of the attack in relation to the day of admission

to hospital. The mortality rate in coronary occlusion is highest in the first few days after the attack; therefore the longer the average delay before admission to hospital, the lower will be the mortality rate of the series. In this series 35 (61%) of the "controls" and 45 (66%) of the "treated" patients were in hospital within twenty-four hours of the onset of their attacks (Table IV).

Shock.

Accuracy in assessing the results of treatment requires also that a proportional number of severe cases be included in each group. Unfortunately, there is no accurate clinical method of measuring the severity of an attack for statistical purposes, but the degree of shock gives some indication.

TABLE III.
Preexisting Heart Disease.

Earlier Cardiac Disorder.	Males.		Females.	
	Controls.	Treated.	Controls.	Treated.
Previous angina	14	13	5	7
History of dyspnœa or congestive failure	5	2	2	1
Previous coronary occlusion	7	9	1	2

The degree of shock has been estimated from the clinical notes, which were not invariably clear on the point; therefore the following figures are not entirely reliable.

Severe shock occurred in 12% of the "controls" and 13% of the "treated". Moderately severe shock was present in 12% and 16% respectively, and it was slight or absent in 76% and 71% respectively.

TABLE IV.
Duration of Symptoms before Admission to Hospital.

Time of Admission to Hospital.	Controls.	Treated.
First day	35	45
Second day	2	4
Third day	1	9
Fourth day	4	0
Fifth day	1	1
Sixth day	1	2
Seventh day	1	1
Second week	3	1
Third week or later ..	9	3
Total	57	68

These figures suggest an even distribution. Absence of shock, however, does not invariably indicate that the attack has been a mild one. Some patients may have been too ill to be transported to hospital until the shock had passed off. When both groups are taken together, eight patients died who had suffered from severe or moderately severe shock when first examined, whereas shock had been slight or absent in 18 patients who subsequently died.

There had been delay in admission to hospital in 11 of these 18, so that seven patients had been examined early in their attacks yet had shown no sign of shock. Persistent congestive failure was present in three of the seven, but the remaining four never appeared to be very ill, and the outcome could not have been predicted. There were two in each group.

Friction.

The presence of friction, denoting pericarditis, had no bearing on the severity of the attack, nor did it assist in prognosis. Friction was reported in four of the 26 fatal cases and in 11 of the non-fatal cases. Pericarditis was found two or three times at autopsy when it had not been noted clinically.

So far, we have seen that the two groups of patients—the controls and the treated—are comparable in respect of age, sex, preexisting heart disease, duration of attack before admission to hospital, and severity of the illness. There may be other factors which cannot be assessed—for example, the omission of some important event from the clinical notes, or an unspecified but valid reason for withholding treatment with dicoumarol.

Thrombo-embolic Complications.

Thrombo-embolic complications occurred in 12 cases (10%). It was surprising to find that these complications were recorded in relation to only five of the controls and seven of the treated. There were nine instances of pulmonary infarcts (multiple in two cases), and three cerebral infarcts.

TABLE V.
Analysis of Deaths.

Age. (Years.)	Male Patients.		Female Patients.	
	Controls.	Treated.	Controls.	Treated.
35	0	1	0	0
40	0	0	0	0
45	1	0	0	0
50	0	0	0	0
55	2	0	0	1
60	1	2	1	0
65	3	1	0	1
70	5	1	1	1
75	2	0	2	0
Totals ..	14	5	4	3

One patient developed hemiplegia and multiple pulmonary infarcts, another phlebothrombosis and pulmonary emboli.

There were five deaths among these 12 cases (two "controls" and three "treated" patients), but only one death was directly due to thrombotic episodes. This patient, who had not been given dicoumarol, died as the result of multiple pulmonary emboli; this was confirmed *post mortem.*

TABLE VI.
Time of Occurrence of Death from Onset of Symptoms.

Time.	Controls.	Treated Patients.
First week	6	2
Second week	3	2
Third week	2	0
Fourth week	3	1
Fifth week	0	0
Sixth week	3	2
Ninth week	1	1
Total	18	8

Diagnosis.

The diagnosis was confirmed by electrocardiography in all but two cases, and in these it was proved *post mortem.*

The presenting symptom of pain in the chest was present in all except 16 of the 125 cases. The pain was felt in the epigastrium in five cases, leading to delayed diagnosis on one occasion. "Painless occlusion" accounted for eight others, in which the main complaint was breathlessness of sudden onset. The remaining three patients were admitted to hospital in coma. Premonitory symptoms of occlusion —that is, aggravation and prolongation of anginal pain occurring during rest—were noted several times. This condition persisted for one to fourteen days.

Dyspnœa, crepitant rales over the lung bases, and cyanosis, suggesting left ventricular failure, were found on numerous occasions on the first examination. These signs were sometimes present without much shock.

White cell counts were not very helpful, because although they usually revealed an increase, the numbers were often within normal limits.

An estimation of the serum cholesterol content was made on 21 patients. When the upper normal limit was taken as 250 milligrammes *per centum*, the serum cholesterol content was found to be raised in 12 cases. In two of these *diabetes mellitus* was present.

A slight to moderate elevation of temperature during the first few days was present in 90 cases (72%).

Results of Treatment.

There were 26 deaths in the period during which these 125 patients were in hospital; 18 in the "control" group of 57, with a mortality rate of 31·5%, compared with eight in the "treated" group of 68, with a mortality rate of 11·8%.

Table V shows the age and sex of those who died and whether they had been treated with dicoumarol or not. The highest death rate was among those who had reached the age of seventy years.

Table VI indicates the duration of the illness until death in each group, the highest death rate being in the first week.

Mode of Death.

Ten patients died of congestive heart failure. Sudden death accounted for eight others, six of whom had reached what appeared to be a safe convalescent stage. At autopsy, rupture of the heart was found in two of the latter—both in the treated group. Embolic complications claimed only one victim, and recurrent myocardial infarction occurred once only. Persisting shock was the cause of death in two cases. In the remaining four cases, the mode of death was not specified (Table VII).

TABLE VII.
Mode of Death.

Mode of Death.	Controls.	Treated Patients.
Heart failure	7	3
Sudden death	4	4
Persisting shock.. ..	1	1
Recurrence of infarct ..	1	0
Pulmonary infarcts ..	1	0
Unspecified	4	0

Comment.

This method of comparison between treated and control patients after and not during the time when they were under observation is open to criticism, because so much depends on the accuracy of the clinical records.

For example, it seems unlikely that thrombo-embolic complications should be met with more frequently among the patients who had been treated by an anticoagulant than among the controls.

Such an authority as Irving Wright regards the beneficial effects of dicoumarol as chiefly due to a reduction in thrombo-embolic deaths. However, in the present study, 15 of the 26 patients who died were examined *post mortem*, and only one death was found to be due to emboli.

There seems little doubt that dicoumarol has a powerful vasodilator action on the coronary arteries (Fantl, 1949), and it may well be that this action is just as important as its anticoagulant effect.

Conclusion.

Although these figures are highly suggestive, I believe that we should accept them with some reserve and defer final judgement until we have a larger series.

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Reports of Cases.

SYRINGOCYSTADENOMA ASSOCIATED WITH ICHTHYOSIS.

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THE first case of what was later called syringocystadenoma to appear in the literature was under the name of *lymphangioma tuberosum multiplex*; this patient was examined by Kaposi at his Vienna clinic in 1867; sections of one of the lesions were prepared and microscopically examined by Biesiadecki who noted multiple tiny cystic spaces in the dermis, which he mistakenly thought were lined by endothelium and not epithelium, with some increase in the connective tissue around them; the spaces contained an amorphous material, not blood; and he considered the tumours to be of lymphatic origin, hence the

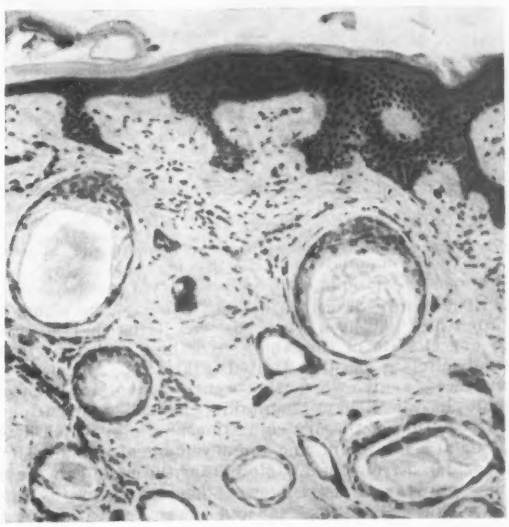

FIGURE I.
Photomicrograph of a stained section of the biopsy material from H.W.H. (× 100).

name given. Kaposi described this case with illustrations in Hebra's *"Lehrbuch der Hautkrankenheiten"* (1872 and later), of which a copy translated by C. Hilton Fagge and Waren Tay on behalf of the New Sydenham Society is available in the library of the New South Wales Branch of the British Medical Association in Sydney; Hebra's *Lehrbuch* in turn appears to have been part of Virchow's *"Handbuch der speciellen Pathologie und Therapie"*.

In 1887 Jacquet and Darier described the same condition under the name of *hidradénomes éruptifs*, and considered it to be of sweat duct origin; in the same year Brocq (1887) in the same journal described the condition under the name of *epithéliomes kystiques bénins* (benign cystic-epithelioma).

In 1889 Török described the same condition again under the name of syringocystadenoma.

In 1892 Fordyce described and named the condition of multiple benign cystic epithelioma, as we now recognize it, and in the same year Brooke gave a description of the latter condition under the name of *epithelioma adenoides cysticum*. These two authors included cases of syringocystadenoma as belonging to the clinical entity they were describing, and for a time after this dermatologists seem to have regarded syringocystadenoma as a variety of multiple benign cystic epithelioma; but in 1900 Neumann separated again the condition that is the subject of this article and called it syringocystoma.

In 1904 in Italy, Fiocco described it under the name of syringoma.

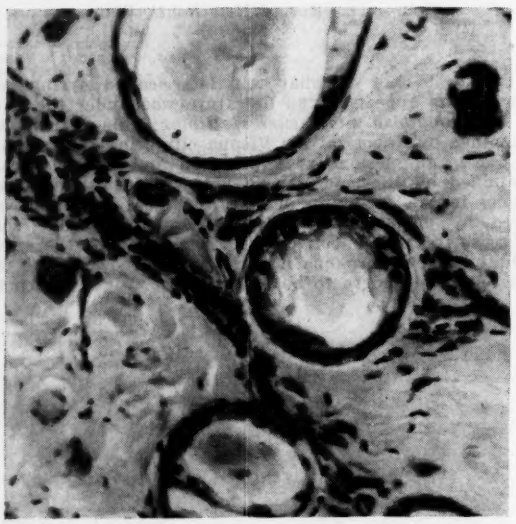

FIGURE II.
Photomicrograph of a stained section of the biopsy material from H.W.H. (× 200).

In 1907 White described a case in a girl, in whom the eruption first appeared when she was living in 1896 in the high dry climate of the Andes, remained quiescent in the normal climate of the United States of America, and recrudesced again when she went to another high dry climate in the Rocky Mountains; he called attention to the association of the dry cold atmosphere, in which sweating was at a minimum, and the development of the lesions; he considered from the histology that the papules were due to new growths of efferent sweat ducts with cystic dilatations. This patient had noticed normal sweating of the neck region, but diminished sweating in the axillæ, where the lesions were mostly situated.

In 1912 Sutton and Dennie came to the conclusion that syringocystadenoma was an innocent tumour arising in misplaced embryonal coil gland (sweat gland) elements, and this view is still generally accepted; Wiedman and Besançon (1930) agreed with this view, but also suggested a possible apocrine gland origin, which Homma and Escher (1936) appear to consider certain rather than possible. Many are the names for rare skin diseases, and yet other names for this condition are *nævus syringadenomatosus*, *cellulome epithéliale éruptif*.

Syringocystadenoma and Multiple Benign Cystic Epithelioma: Differential Diagnosis.

We may still doubt even now whether syringocystadenoma and multiple benign cystic epithelioma may not be the same.

Howard Fox, in 1923, in a discussion on syringocystoma, considered that it had a distributive predilection for the chest and was of sweat gland origin, while multiple benign cystic epithelioma had a predilection for the face and had origin in connexion with the hair follicles. He said that the cysts of syringocystoma were formed of branching anastomotic ducts not connected with the skin surface, whereas normal coil gland ducts in the same patient could be traced to the surface.

The following table (Table I) for differential diagnosis contains points from various authors that may be helpful; with regard to prognosis, syringocystadenoma is apparently completely innocent, while benign cystic epithelioma, though usually innocent, very rarely becomes malignant.

TABLE I.

Characteristic.	Syringocystadenoma.	Multiple Benign Cystic Epithelioma.
Preferential distribution.	Chest and axillæ.	Face.
Colour ..	Flesh-coloured, with tendency to brown or fawn or red.	Flesh-coloured, with tendency to blue or whitish-yellow.
Macroscopic appearance.	Smooth papules, with lack of "pearly" elements, but there may be a waxy appearance.	Smooth papules, sometimes with a "pearly" appearance.
Telangiectases..	None.	May sometimes be seen, adjacent to lesions.
Ulceration ..	Never present.	Rare, and if it occurs suggests developing basal-cell epithelioma.
Microscopic appearance.	Multiple cystic spaces in the dermis with typical lining of an inner layer of cubical epithelium and an outer layer of flattened cells, though there may be more epithelial layers; the cysts contain "colloid", an amorphous albuminous substance; there may be a few groups or columns of cells apart from the cysts, or attached like the tail of a comma, or the cyst itself may have a "comma" shape.	Multiple layers of epithelial cells in groups or columns in the dermis, some related to hair follicles; some with cystic spaces lined by several layers of epithelial cells. The cysts may contain colloid, or sebaceous material, or even keratinized whorls, and they also may have a tailed "comma" appearance.

Relationship of Syringocystadenoma to Ichthyosis.

There is probably more than a coincidental association between ichthyosis and syringocystadenoma, for both syringocystadenoma and ichthyosis seem to be traceable to congenital anomalies, and the dry scaly cornified skin of ichthyosis may hinder sweating from normal sweat glands and ducts, but encourage proliferation of the cells of embryonic sweat glands.

White (1907) has previously noted the occurrence of syringocystadenoma associated with dry skin and diminished sweating.

Clinical Record.

H.W.H., a man, aged thirty-nine years, was examined in June, 1950, for life assurance by a medical practitioner who reported a generalized dry dermatitis which "might necessitate special terms for acceptance". He was referred to me by the office for opinion, and I found a condition of mild generalized ichthyosis, present as long as the proponent could remember. In addition to this, however, I observed a number of slightly elevated, smooth, rounded, firm papules, almost flesh-coloured but with a reddish-purple tinge, each about 0·3 to 0·5 centimetre in diameter, on the front of the chest, the upper part of the abdomen, and the lower part of the neck. The proponent said he had noticed these for about two years, and that they had not changed in appearance during that time, but occasionally new ones

had appeared; they caused no inconvenience. I considered that a biopsy of one of these papules was necessary for diagnosis and referred him to Dr. Francis Thompson, who excised a papule and sent it to Dr. A. H. Tebbutt for section and microscopic examination. The lesion was found to be syringocystadenoma.

Histology of Lesion of H.W.H.

In Figures I and II are seen reproductions of photomicrographs of a stained section of the biopsy material from H.W.H. The multiple cystic spaces in the dermis can be well seen, lined by epithelium of which the general structure is an inner layer of cubical cells and an outer layer of flattened cells; the amorphous colloid content of the cysts is seen.

Parts of some of the cyst walls contain more than two layers of cells; there are some grouped cells in the dermis apart from the cysts, mostly small round cells and connective tissue cells, but there may be some epithelial cells among them.

Acknowledgements.

I wish to express my thanks to Dr. F. Thompson and Dr. A. H. Tebbutt for their opinion and biopsy, to Mr. Woodward-Smith and the Department of Medical Artistry, University of Sydney, for the photomicrography; to Miss M. Rolleston, librarian of the British Medical Association library at Sydney, for much help in obtaining ancient volumes from the vault; to the Director-General of Health, New South Wales, and to the general manager of the Government Insurance Office, for permission to publish this report.

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Reviews.

DIOPHTHALMOLOGY.

THE small thesis "Introduction to Diophthalmology" is presented by N. A. Stutterheim to amplify his former publications.[1] He considers that in every-day life our perception of space, immediate, direct, three dimensional, is pure and perfect. The diophthalmos masters the third dimension of the visual environment by functional trigonometry—from the transverse disparity of the angles of the visual lines joining each object to the centres of rotation of the right and left eyes.

The author believes the muscular activity of convergence to be of the greatest importance for binocular vision and its depth perception. That depth perception is accurate in flashes shorter than the refractory period of muscle is explained by the eyes being kept continually on the alert in tonic convergence on some nearby point unseen in the dark.

The author deplores the experiments and reasonings current since ophthalmology became a specialty. He dismisses the conception of disparate images and the artificial workings of instruments such as the stereoscope as these have lost touch with vital reality. Unfortunately many conclusions are presented without sufficient factual foundation.

SQUINT.

BRITISH OPHTHALMOLOGY has been fortunate in having had a Worth and a Chavasse and now in having a Lyle. To Lyle has been entrusted the task of writing the eighth edition[1] of "Worth and Chavasse's Squint". This new edition is a clear exposition of the theories of squint and is enriched by a clarity of expression which has rendered more understandable many of the doctrines outlined by Chavasse in the seventh edition. The chapters on investigation and treatment are excellent, showing a proper balance between non-surgical, including orthoptics, and surgical treatment. The chapter on surgical treatment is good, reflecting Lyle's vast experience. Here the reader will learn why a given procedure does not give a constant correction; the surgeon will find guiding principles which are invaluable. Berke's operation on the superior oblique is fully described, and it is gratifying to see that the operation for the cure of lateral rectus palsy is referred to (among other names) as Temple Smith's operation. The text-book is well produced, contains many illustrations and will more than ever be the standard work on squint.

OBSTETRICS AND GYNÆCOLOGY.

F. J. BROWNE needs no introduction to those in Australia who practise obstetrics and gynæcology. His fresh work "Postgraduate Obstetrics and Gynæcology"[2] was therefore read with anticipation and pleasure.

The book covers many aspects of obstetrics and gynæcology, but omits certain important subjects which had been covered in the author's previous work, "Ante-natal and Post-natal Care". Although intended for post-graduates, the book opens with an elementary introduction on pelvic anatomy and function, and the development of the placenta and ovum. From this it is a logical step to his discussion of abnormalities of the female genital tract, which, though brief, gives with adequate diagrams a good working knowledge of these conditions.

Three chapters are devoted to inflammatory states of the genital tract, including tuberculosis, gonorrhœa and trichomonas vaginitis. An up-to-date review of venous thrombosis gives pleasing prominence to the "Sydney work" of Cummine and Lyons.

There is a good chapter on the "Third Stage of Labour and Post-partum Hæmorrhage". Browne makes an interesting comment on the use of ergot or posterior pituitary extract after the child's head is born and before delivery of the placenta. As to ergot, his conclusion is brief and to the point—"it seems to do neither good nor harm". The use of posterior pituitary extract, however, "seems to be much more apt to cause a constriction ring". Two brief chapters only are devoted to the toxæmias; this subject is one of the important items which Browne has adequately covered in his "Ante-natal and Post-natal Care".

Among the subjects on the gynæcological side, Browne deals with amenorrhœa, dysmenorrhœa, endometriosis and tumours and makes an extensive reference to pelvic cancer.

[1] "Introduction to Diophthalmology", by N. A. Stutterheim, M.D. (Rand.), with a foreword by W. P. C. Zeeman, M.D.; 1950. London: H. K. Lewis and Company, Limited. 8½" × 5½", pp. 56, with two graphs. Price: 7s. 6d.

[1] "Worth and Chavasse's Squint: The Binocular Reflexes and the Treatment of Strabismus", by T. Keith Lyle, C.B.E., M.A., M.D., M.Chir. (Cantab.), M.R.C.P. (London), F.R.C.S. (England); Eighth Edition; 1950. London: Baillière, Tindall and Cox. 10" × 7¼", pp. 332, with 200 illustrations. Price: 35s.

[2] "Postgraduate Obstetrics and Gynæcology, 1950", by F. J. Browne, M.D. (Aberdeen), D.Sc., F.R.C.S. (Edinburgh), F.R.C.O.G.; 1950. London and Australia: Butterworth and Company (Publishers), Limited. 9½" × 6½", pp. 552, with 107 illustrations. Price: 65s.

There is an interesting but brief chapter on intersexuality and a well-written one on congenital malformations. The following 72 pages are devoted to a mixture of both obstetrical and gynæcological subjects. To mention a few which make good reading, there are "Heart Disease in Pregnancy", "Stress Incontinence", "Anuria", "Rupture of the Uterus" and "Failed Forceps".

McClure Browne closes the work with three brief chapters devoted to "Pre-operative and Post-operative Care" and "Blood Transfusion".

F. J. Browne's book can be recommended as a useful and most readable addition to the post-graduate library of any doctor practising obstetrics and gynæcology and particularly to those studying for a higher degree in these subjects. It will receive a particularly warm welcome in Australia following "F.J.'s" successful lecturing tour of this country in 1950 when he was Visiting Lecturer for the King George V and Queen Mary Maternal and Infant Welfare Foundation of New South Wales.

ORTHOPÆDIC SURGERY.

THE appearance of the fourth edition of the well-known "Orthopædic Surgery" by Professor Walter Mercer[1] will be welcomed alike by orthopædic and general surgeons and by general practitioners, for this work has in the past been very extensively read and quoted. The present edition is larger than the last and some of the chapters have been completely revised to bring them up to date. One masterly chapter is that dealing with the subject "Some Complications of Trauma", in which such entities as Volkmann's ischæmic contracture, non-union of fractures, and the problem of the stiff knee are discussed fully. As these topics are some of the everyday problems confronting both specialists and general practitioners, the practical advice for either avoiding or correcting these complications is most useful. Among various procedures of his own devising, the author discusses his technique for menisectomy, using his own special chisel-shaped knife.

It is proof of the completeness of the book to mention that chapters are devoted to the various muscular dystrophies and atrophies as well as to circulatory disease of the extremities, for while these are always found in textbooks of medicine, they are not always included in orthopædic works.

Some 427 illustrations add practical points to the text, which throughout is clear and comprehensive while always being essentially practical. It is a pleasure to recommend such a book.

STEROID HORMONES AND TUMOURS.

"STEROID HORMONES AND TUMOURS" is a summary of the valuable work of Lipschutz and his associates in the field of the "tumorigenic" effect of œstrogens.[2] It is a work which is far more suited to the requirements of the researcher in the cancer field than to the profession in general, but nevertheless many points arise which must give the practitioner furiously to think, especially in these days of enhanced hormone consciousness. We quote: " . . . Our first experiments were made with the 3-benzoic ester of α-estriadiol; this ester was at that time preferably used by the practitioner. . . . We were able to elicit fibroids with all the compounds tried." The author very properly draws attention to the objection raised by the clinicians that the quantities administered were larger than the potentialities of the ovary even under pathological conditions, but this objection seems fairly answered in the context.

The discussing centring around the dynamics of carcinogenesis, with reference to the hormonal, viral and chemical carcinogens, are of particular interest in view of recent theories propounded in this field.

The chapters dealing with hormonal treatment of tumours and "antitumorigenic" steroids are rather difficult to read, but repay the effort, and in the author's own summing up: "We are fully aware that it is not possible to apply to humans all those experimental results which have been obtained in laboratory animals. The behaviour of homologous territories in different animal species . . . varies enormously. . . . It is to the practitioner, and in the first place to the gynæcologist, to decide how far use can be made . . . for the benefit of man."

If we take into consideration the fact that the work is a translation, and that the author has not that proper reverence for the purity of the English language which is desirable even in technical works ("tumorigenic" in any language would, we feel, come under the heading of "mongrel"), the book is well written, well and copiously illustrated by photographs, and attractively presented. It is an essential book of reference in any cancer research department, and should have a special appeal to the gynæcologist.

SECTION CUTTING AND STAINING.

THE appearance of a second edition of "Practical Section Cutting and Staining" by E. C. Clayden, senior technician in the Morbid Histology Department of the Bland-Sutton Institute of Pathology, the Middlesex Hospital, London, shows that this small book has proved its usefulness.[1] It is written essentially for technicians with little or no experience in the various methods of preparing routine sections. The directions given are clear, simple and very detailed. Section cutting by the Cambridge rocking microtome is described; rotary microtomes are mentioned and such modern labour-saving devices as the "Autotechnicon" are not mentioned. Perhaps this omission is deliberate; it is certainly more important for the beginner to learn to be a good craftsman than to read about elaborate mechanical devices. On the whole this book is more suitable for use in small laboratories than in larger centres. This edition includes some new methods including the rapid preparation of bone sections.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Cry and the Covenant", by Morton Thompson; 1951. London: William Heinemann (Medical Books), Limited. 8" × 5¼", pp. 502. Price: 18s. 9d.

A novel about Semmelweis and the fight against puerperal infection.

"Nutrition and Chemical Growth in Childhood", Volume III, Calculated Data, by Icie G. Macy, Ph.D., Sc.D., with a foreword by Helen A. Hunscher, Ph.D.; 1951. Springfield, Illinois: Charles C. Thomas. 9" × 6", pp. 728. Price: $2.00.

A selection of calculated data, considered to be that of greatest possible use and interest, taken from the results of interpretation of studies of nutrition and chemical growth in childhood.

"Tropical Nutrition and Dietetics", by Lucius Nicholls, C.M.G., M.D., B.C., B.A. (Cantab.); Third Edition; 1951. London: Baillière, Tindall and Cox. 9" × 6¼", pp. 486, with 57 figures and 17 graphs. Price: 42s.

A new edition of a book intended to cover the general principles of nutrition and dietetics especially in relation to the tropics, and to collect together the scattered salient points on the subject.

"Baillière's Nurses Medical Dictionary", revised by Margaret E. Hitch, S.R.N., with a foreword by Sir Cecil Wakeley, K.B.E., C.B., D.Sc., F.R.C.S.; Twelfth Edition; 1950. London: Baillière, Tindall and Cox. 5¼" × 3⅜", pp. 508, with 180 figures. Price: 5s.

A useful book intended for nurses, "V.A.D.'s", Civil Nursing Reserves, members of the Red Cross and of the St. John Ambulance and for first-aid workers.

[1] "Orthopædic Surgery", by Walter Mercer, M.B., Ch.B., F.R.C.S. (Edinburgh), F.R.S. (Edinburgh), with a foreword by Sir John Fraser, Bart., K.C.V.O., M.C., F.R.S.Ed., F.R.C.S.Ed., M.D., Ch.M., F.R.A.C.S., F.A.C.S.; Fourth Edition; 1950. London: Edward Arnold and Company. 9" × 5¼", pp. 1032, with many illustrations. Price: 50s.

[2] "Steroid Hormones and Tumours: Tumorigenic and Antitumorigenic Actions of Steroid Hormones and the Steroid Homeostasis Experimental Aspects", by A. Lipschutz, M.D.; 1950. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" × 5¾", pp. 328, with many illustrations. Price: 64s. 6d.

[1] "Practical Section Cutting and Staining", by E. C. Clayden, F.I.M.L.T.; Second Edition; 1951. London: J. and A. Churchill, Limited. 8" × 5", pp. 148, with 23 illustrations. Price: 10s.

The Medical Journal of Australia

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Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

CHRONIC BARBITURATE INTOXICATIONS AND ADDICTIONS.

No one who has anything to do with the practice of medicine or the dispensing of drugs will question the statement that the use of barbiturates has grown by leaps and bounds, but one wonders whether its full extent is realized even by medical practitioners. In the report of an experimental study on chronic barbiturate intoxication, Harris Isbell, writing with five collaborators from the Research Division of the United States Public Health Service,[1] states that in 1948 the total production of barbiturates in the United States was 672,000 pounds, an amount equivalent to 3,057,730,000 capsules or tablets of 0·1 gramme each, or approximately 24 doses for each person in the United States. It will no doubt be held that the extensive use of sedative drugs is a sign of the speed of present-day life and of the nervous tension at which most people live. This may be partly true, but there is no doubt that some people like these drugs and become habituated to them and so will go to any lengths to obtain them. Further, it is doubtful whether the medical profession is not partly to blame for the present state of affairs—whether its members have always been wise in their prescribing of barbiturates and in trying to withhold from patients the knowledge of what their prescriptions hold. However that may be, Isbell states that acute intoxication with barbiturates accounts for about 25% of all cases of acute poisoning among patients admitted to general hospitals, and that more deaths are caused by barbiturates, either accidentally ingested or taken with suicidal intent, than by any other poison. Isbell refers to papers on chronic barbiturate intoxication and on the effects of their withdrawal published in German journals and also to some reports appearing in the United States. He points out that many of the latter are unsatisfactory because the cases were cases of mixed addiction (morphine and alcohol) and it was impossible to tell which symptoms were due to the withdrawal of barbiturates and which were not. Moreover, the physical and mental conditions of the patients before their addiction were not known and it was difficult to determine whether the development of convulsions and psychoses was dependent on an underlying psychotic or epileptic diathesis. In order to obtain clear-cut information he carried out an experimental investigation on five men who had been morphine addicts. These men were volunteers who were serving sentences for violation of the *Narcotic Act*. None had significant physical defects and all had normal electroencephalograms. They had all served more than one sentence for violation of the *Narcotic Act* and all had long records of alcoholism. In the past each had had at least one psychiatric examination and the presence of a character disorder had been diagnosed.

The subjects received doses of secobarbital ("Seconal"), pentobarbitol or amobarbital ("Amytal") sufficiently large to induce continuous mild to severe intoxication for periods varying from ninety-two to one hundred and forty-four days. Five doses were given in each day. The dose was increased from the first to the twenty-first day, and from then to the end of the period of "chronic administration" the increase was much less. The symptoms of chronic intoxication included impairment of mental ability, confusion, regression, increased emotional instability, nystagmus, dysarthria, ataxia and depression of the superficial abdominal reflexes. The clinical manifestations were similar to those of chronic alcoholism. Curiously, the effect of a certain dose varied greatly in the same person from day to day and this variation was partly related to changes in food. The same dose of barbiturate produced considerably different effects in different individuals. By means of variation in dosage at the end of the period of "chronic administration" it was concluded that a certain amount of tolerance developed during chronic intoxication. Withdrawal symptoms occurred in all instances. During the first twelve to sixteen hours after the last dose of barbiturate had been given the condition of all five patients appeared to improve, confusion became less and neurological manifestations almost disappeared. After this they began to complain of vague anxiety and of increasing weakness. They slept poorly, ate little and had a coarse tremor of the face and hands. Twenty-four to thirty hours after the last dose of the drug anxiety became severe and weakness was so great that the patients could hardly stand or walk. They felt faint and preferred to remain in bed. Tremor increased and in four instances fasciculation of isolated muscle groups was seen. Four of the subjects vomited. The patients were mentally clear and well orientated and showed no evidence of hallucinations at this time. Four of the patients had convulsions after varying periods of abstinence. Four patients developed psychoses which resembled *delirium tremens*. Recovery appeared to be complete and no clinical evidence of permanent damage was detected sixty days or more after withdrawal began. The evidence presented by Isbell and his co-workers makes it quite clear that the barbiturates are addiction-forming drugs. Addiction to morphine is always looked on with horror and is thought to be a serious affliction. Isbell holds that the manifestations of chronic barbiturate intoxication are in most ways much more serious than those of addiction to morphine. Morphine, he points out, causes much less impairment of mental ability and

[1] *Archives of Neurology and Psychiatry*, July, 1950.

emotional control and produces no motor incoordination. He adds that such impairment as does occur with morphine becomes less as tolerance to morphine develops and withdrawal of morphine is less dangerous than withdrawal of barbiturates. The evidence offered by Isbell suggests that his views are correct. He points out that recovery from barbiturate addiction appears to be complete; one wonders whether the recovered morphine addict will not be more liable to relapse than a person recovered from barbiturate addiction. If this proved to be the case morphine would in the opinion of many be the more dangerous drug.

Isbell's account of his experimental study is reinforced for the clinician by another contribution from him.[1] At the annual meeting of the American College of Physicians in April, 1950, he presented a paper on addiction to barbiturates and the barbiturate syndrome which is of more practical use to the practitioner. We do not propose to deal with this in any detail, but would draw attention to one or two points. The persons likely to become addicted to barbiturates are those with psychoneuroses or character disorders. Many become addicted after they have received prescriptions for insomnia. Isbell insists that this reflects the mistaken idea that barbiturates are not habit-forming drugs. He has shown by his experiments that they are. We have to remember that there is a great difference between the administration of the drugs to Isbell's subjects and the administration of barbiturates even for long periods to patients who are under the control of their doctors. Isbell's subjects all were of the type described by him as suitable candidates for addiction; they received for many days doses of barbiturates varying in four instances from 20 to 27 grains a day and in one instance up to 57 grains a day; they were all alcoholics. Some clinicians would say that he over-emphasizes his arguments; the reply to that would be that to understate the case is dangerous. To suggest the elimination of barbiturates from medical practice would be as absurd as to think that doctors could dispense with opiates. Countless patients owe it to barbiturates that they are able to make a brave showing in the face of upsets and deficiencies in themselves or their environment. It is control that matters and common sense in the issuing of "repeat" prescriptions. Isbell states that alcoholics are likely to begin the use of barbiturates, perhaps at the instance of a medical practitioner, to relieve the nervousness following on a long debauch. They find that the effects are similar to those of alcohol and continue to use the drugs in order to induce intoxication and not to relieve nervousness or insomnia. Medical practitioners must see that they can never be held responsible for this kind of behaviour—of all illnesses the iatrogenic are most to be avoided.

Current Comment.

THE DURATION OF GESTATION.

THE duration of gestation is a matter of practical importance in all cases to both the mother and the obstetrician. In special cases it can have considerable medico-legal implications. Curiously enough data of value on the subject are rather limited. A useful contribution to the subject has been made by J. R. Gibson and Thomas McKeown,[1] as the result of an inquiry into all the births that occurred in Birmingham in 1947. The data on these births by their number (23,970) and their inclusive nature are free from the criticism to which most other data are open—namely, that the observations are confined to hospital births (a selected group) and that the numbers are too small to permit adequate examination of the distribution. Our present knowledge of the duration of gestation in man, Gibson and McKeown point out, may be summarized in the statement that the mean is firmly established as approximately 280 days, but there is insufficient knowledge of the nature of the distribution, and of its association with such variables as maternal age, parity and birth weight. The present paper deals with the duration of gestation of single births, and with its relationship to maternal age and parity. The duration of gestation was estimated from the date of the first day of the last menstrual period as recorded on documents prepared during the antenatal period. This information was available for 17,384 (74·7%) of the 23,279 single births. It was found that the mean durations of gestation for domiciliary and nursing-home births did not differ significantly, being approximately 281 days; both were a little longer than the mean for hospital births (approximately 280 days). When all births (domiciliary, hospital and nursing home) were considered together, the mean durations of gestation were as follows: live births, 280·85 days (± 0·12); stillbirths, 267·27 days (± 1·35); total births, 280·52 days (± 0·12). Of all births 28% occur in the fortieth week and 65% in the thirty-ninth, fortieth and forty-first weeks. That is to say, about one-third of all births occur earlier than the thirty-ninth or later than the forty-first week of gestation. The greatest recorded duration of gestation in the series was fifty-one weeks, of which there were two examples (0·01% of the total); one was associated with a live birth, the other with a stillbirth. Two live births occurred in the fiftieth week. From their data Gibson and McKeown have constructed a simple table which shows the expected dates of delivery for pregnancies that have completed a stated number of weeks. The table provides, of course, only group probabilities—no table could give more—and the individual pregnancy under consideration may always be one of those outside the main group. Nevertheless it will be useful as a guide to the obstetrician, as it takes into account both variation around the mean duration of gestation and changes in the expected date as pregnancy advances; this cannot be said of the customary method of working on the mean of 280 days as if it applied in nearly every case. The other aspect of the investigation recorded in the present paper, consideration of the duration of gestation in relation to maternal age and parity, failed to reveal any consistent relationship. Comments on birth weight, on which a large body of data is available, are reserved for a later communication.

[1] *Annals of Internal Medicine*, July, 1950.

TERRAMYCIN.

AMONG the more recently introduced antibiotics are some which have aroused interest not only by their effectiveness in a wide range of infections but also by reason of their capacity for absorption by the alimentary tract. Patients and medical and nursing attendants alike welcome the relief from the need for using the hypodermic syringe. Terramycin, derived from *Streptomyces rimosus*, has been found to possess bacteriostatic properties over a large number of unrelated infective agents. It is also thermostable and tolerant of variations of pH over fairly wide limits, and though it shares with some other similar substances the disability of causing toxic symptoms in some persons, these are rare and usually take the form of mild gastro-intestinal irritation only. R. J. Sayer, Jean C. Michel, F. C. Moll and W. M. M. Kirby have published a study on the properties of terramycin.[1] They used for the purposes of this investigation the patients suffering from infections

[1] *The American Journal of the Medical Sciences*, March, 1951.

commonly met in a general hospital, and treated in all 108 adults and children. Of these, 28 had urinary tract infections, 38 bacterial pneumonia, 21 pertussis, six tonsillitis, four bacillary dysentery, and the remainder of 11 patients had miscellaneous infections which included one case of amœbiasis, one of typhoid fever and one of subacute bacterial endocarditis. All the microorganisms isolated were tested for sensitivity to terramycin; very few were insensitive, one important exception being *Entamœba coli*, which was found as an infective agent in several patients with inflammations of the urinary tract. The antibiotic was rapidly absorbed after oral administration, and antibacterial activity was observed in the serum within an hour after it was given. Very little difference was noticed in the concentrations attained by giving terramycin to patients who were fasting or who had recently taken food, and the maximum concentration was reached in the serum within two to three hours. The drug began to disappear from the blood after about four hours, and traces were still found after twenty-four hours. One gramme of terramycin given by mouth every six hours usually maintained blood levels of 5 to 10 micromilligrammes per millilitre throughout a twenty-four-hour period. The authors have obtained a satisfactory intravenous preparation which produces and maintains adequate blood levels. Blood levels with terramycin have been found to be considerably lower than those obtained with chloramphenicol, but much the same with aureomycin, though terramycin did not deteriorate so rapidly as aureomycin, and was therefore more effective on the whole with comparable concentrations. Chloramphenicol has the further advantage that it is eliminated from the body more slowly. The results with terramycin in urinary tract infections were similar to those obtained with other antibiotics; there were the same not infrequent relapses due to the limitations of bacteriostatic action in the presence of anatomical complications such as obstruction, and also the same occasional development of bacterial resistance. Good response was obtained in pertussis, and as in the reports of other similar drugs used in this disease the authors' records show that the severity of the condition was diminished, and pulmonary complications were controlled. Bacterial pneumonia in children and adults was well controlled also by this agent. The numbers of miscellaneous infections treated were too small to be conclusive, but the single cases mentioned above gave reason for encouragement, and two patients with mumps and one with infectious mononucleosis showed prompt improvement. It is obvious that larger and controlled series of these varied infective states are needed before accurate appraisal can be made, but it would appear that in terramycin we have another bacteriostatic agent which is effective when given by mouth and has earned a place in the antibiotics. It may be that possession of a number of potent agents of this kind will yet help us to solve the problem of resistance.

THE EFFECT OF ASCENDING STAIRS ON THE WORK OF THE HEART.

THE ascent of a staircase has been regarded as a rough but useful test of cardio-respiratory capacity, since it is a standard type of exertion, the only variants for a given individual being the number of steps and the rate of ascent. The subject of a circulatory disability is usually conscious of deterioration or improvement in his performance, and this has also been used as an exercise tolerance test. Indeed, an over-eager patient, demonstrating this method as a means of measuring the exertion which could be expended in anginal subjects without causing pain, once dismayed his doctor and the audience at a clinical meeting by inducing an attack of angina which worried all who saw it. An interesting study has been carried out by J. A. L. Mathers, H. L. Griffeath, R. L. Levy and J. L. Nickerson on the effect on the work performed by the heart during the ascent of a conventional staircase.[1] The series studied was small, but was carefully controlled with an equal number of normal persons. Five patients with coronary disease were tested, two of whom had healed infarcts of the heart, and the others demonstrable coronary insufficiency. Routine investigations were made, including full history, electrocardiogram, X-ray examination and blood count. The cardiac output was determined by the ballistocardiograph, tested by comparison with the Fick method. It is interesting that more than 4000 ballistocardiograms were taken even with this small number of subjects. Heart rates and blood pressure readings were recorded before and after every phase of the investigation, and each patient's performance was controlled by repetition of the tests both with and without exercise. Three types of exercise were used: walking up one flight of stairs, walking down one flight of stairs, and walking down the hall and into the laboratory for an equivalent distance. The person tested was allowed to select his own rate of performance, and the effect of decreasing or increasing this was also observed. The ballistocardiograph was distant 34 feet from the last step; therefore a control was used in which the patient was carried on a stretcher to the top of the steps and then walked to the table. The results were considered statistically, for the number of observations was large. As might be expected, ascent of the stairs caused a significant increase in the work of the heart. Expressed in percentages, the cardiac work increased by 54, the stroke volume by 32 and the rate by 13 (eight beats per minute). These figures refer to the normal controls. The cardiac patients showed percentage increases as follows: the cardiac work 75 and the stroke volume 44. The rise in the heart rate was only nine beats per minute, which was not statistically significant. The increases caused by walking down stairs were greater in the cardiac group, but they were not significant, and only borderline increases were found after exercise on the level. The effect on the rate at which the exercise was performed did not vary within important limits in the experiments, but the results show that the cardiac patients, probably benefiting from previous instruction, selected the optimum rate for the test. Further, it appeared that a request to modify the rate consciously caused some augmentation of the work of the heart, no doubt owing to an emotional effect. This is in accordance with general experience, which indicates that acts may be performed without effort or distress by the subjects of heart disease which might upset the functional balance of the circulation if to the exertion was added the effects of emotional stress. The instance of the patient mentioned above is probably an example of this, as a standard exercise familiar to the patient is no longer familiar or standard when carried out under the eyes of an audience. The interest of this study lies to some extent in the fact that the physical test is so mild. The authors conclude that the response of their patients to such a test showed that the increased burden on the heart was important, and that the instructed patient may safely select the rate at which he feels most comfortable, as either hurry or deliberate retardation may add to the work asked of the heart.

The staff of the Work Classification Unit of the Adult Cardiac Clinic of the Bellevue Hospital, New York, also publish an interesting analysis of the occupations of the patients attending this clinic.[2] This forms a good pendant to the above. It was found that of 580 adult patients, 45% of the males and 64% of the females were doing full-time work. Naturally the most common occupations were those of housewife, "white collar" worker and unskilled labourer, and it appeared that there was a useful field in the adjustment of some of these workers in relation to their jobs, as most of them admitted that they felt that certain features of their work imposed strain on them. Nevertheless, comparison with the employed population in general showed that the cardiac subjects lost no more time through sickness than other groups. It seems that further study of the factors concerning industrial usefulness of those who have a cardiac disability would be worth while.

[1] *British Journal of Social Medicine*, October, 1950.

[1] *Circulation*, February, 1951.
[2] *Ibidem.*

Abstracts from Medical Literature.

PATHOLOGY.

Neurofibromatosis and Related Lesions.

KEITH INGLIS (*The Journal of Pathology and Bacteriology*, October, 1950) advances the hypothesis that it is not neurofibromatosis as such that is inherited, but the predisposition to neurofibromatosis, a predisposition which is thought to be wide in its application and to influence the development of a great variety of lesions at the basic intrinsic factor level, a less varied group of lesions at the neural intrinsic factor level and a still more restricted group of lesions at the neurofibromatosis level. Lesions representative of all three levels may be present in one and the same individual, and as any of these lesions may lead to other lesions of a secondary nature, the difficulty of assessing the ætiological significance of some of the lesions in any particular patient may be very great. Such lesions of bones as spinal curvature, congenital pseudarthrosis of the tibia and small size of certain individual bones are thought to be related to and to link up with neurofibromatosis at the basic intrinsic factor level. It is suggested that intrinsic factors may play a part in the ætiology of certain examples of a variety of conditions which occur in patients or their close relatives who, though free from neurofibromata, have one or more lesions belonging to the neurofibromatosis complex, namely, neurilemmoma, meningioma, fibroma, lipoma, angioma, tumours of the optic nerve, glial hyperplasia, epilepsy, cutaneous pigmented patches, spinal curvature, congenital pseudarthrosis of the tibia, small size of bones, hydrocephalus and *spina bifida*.

Post-Traumatic Subcutaneous Granulomata Associated with a Crystalline Material.

WILLIAM W. AYRES, WILLIAM B. OBERAND PAUL K. HAMILTON (*The American Journal of Pathology*, March-April, 1951) state that in the tissues removed from seven patients with post-traumatic cutaneous granulomata a crystalline material was present. The foreign material was probably silica. These cases present a clinical and pathological entity characterized by trauma with silica-containing material, with laceration of the skin healing *per primam*, a latent interval of many years, and a rather acute onset of an often tender nodule beneath the scar, which on pathological examination reveals non-caseating tubercles, giant cells of the Langhans type and anisotropic crystalline material. These granulomatous lesions have been mistaken for Boeck's sarcoid of the skin, but may be differentiated by the appearance of the crystalline material and by special stains.

The Cell Type of Secondary Parathyreoid Hyperplasia.

GEORGE E. FRITZ AND OSBORNE A. BRINES (*The American Journal of Pathology*, March-April, 1951) have studied the parathyreoid glands in 61 cases of bilateral renal disease. Seventy-six cases without renal disease provided control material. A definite increase in weight of the parathyreoid glands was found in the case of renal insufficiency. This was proportionate to the severity and duration of the renal damage. A decrease in fat content of the hyperplastic parathyreoid glands was also found. The predominant parathyreoid cell in cases of severe, long-standing renal disease was the clear cell. In the majority of cases of mild renal disease or renal disease of short duration, the parathyreoid glands contained chief cells and clear cells. Transitions between the two types could be seen. Oxyphilic cells were found not to be increased in number. The parathyreoid clear cell is usually predominant in secondary parathyreoid hyperplasia.

Squamous Epithelium in Encysted Hydrocele of the Cord.

E. S. J. KING (*The Australian and New Zealand Journal of Surgery*, May, 1951) describes three cases of hydrocele of the cord with a stratified epithelial lining. Gradations between a single layer of epithelium, through a stratified form, to a squamous stratified type with keratin are demonstrated. The author considers that the relation of these various types is such that a development of the squamous epithelium from the peritoneal cells is one of metaplasia of tissues in adult life.

Biological Predeterminism in Human Cancer.

IAN MACDONALD (*Surgery, Gynecology and Obstetrics*, April, 1951) states that the behaviour of a neoplasm in an individual host is an expression of a biological potential established during the inductive phase of neoplasia. The factors determining the inherent potential of a given neoplasm for growth and dissemination are probably genetic. Thus the balance of power between neoplastic and reactive influences in the host has been established in the preclinical phase of the process, and in a clinical sense this concept may be expressed as that of biological predeterminism. Rigid ideas of therapeutic measures and prognosis in terms of duration and dimension of neoplasia should be abandoned in favour of a search for more accurate criteria of the diverse biological potentialities in human cancer. Such indications of growth potential as are presently available should be applied with the intent of affording curative measures for many patients commonly regarded as presenting "late", and therefore incurable, cancer.

Gastric Changes in Pernicious Anæmia.

LEONARD C. MOLOFSKY AND FRANKLIN HOLLANDER (*A.M.A. Archives of Internal Medicine*, January, 1951) review the literature concerning the pathological changes of the stomach in pernicious anæmia. A considerable lack of uniformity in the descriptive reports exists, but there is general agreement about the following changes. In the body and fundus the mucosa is remarkably thinned and sharply demarcated from the pyloro-antral region. The glandular tubules are greatly altered, having a scattered, irregular arrangement. They are decreased in number and length, but increased in tortuosity, and branching cystic dilatation of the tubules is frequent. The lining epithelium of the glands consists of undifferentiated cuboidal mucus-secreting cells. The specific parietal and peptic cells are rare or entirely absent. Scattered islands of intestinal metaplasia of the mucosa are seen. The interstitial tissue is usually considered to be increased, with an infiltration of numerous lymphocytes, plasma cells, eosinophile cells and Russell bodies. Fibrosis of the interstitial tissue is described by some observers. Atrophy of the submucosa and muscularis has also been noted. In contrast to this, the pyloric and antral region is considerably thicker and reveals only slight gastritic change. Evidence is reviewed that the argentaffin cells are absent in pernicious anæmia and that they may normally elaborate the specific antianæmic factor. There is an increased frequency of both benign and malignant tumours of the stomach in this disease. During relapse, gastroscopic observation reveals changes typical of atrophic gastritis of varying degree. During remission following treatment with liver, the mucosa may be restored in variable degree to a normal gastroscopic appearance, but whether or not this represents restitution to histologically normal mucosa has not been demonstrated. The nature of the gastric lesion is still unsettled, though inflammatory and degenerative processes have been invoked, individually or together, to explain the mucosal atrophy.

Benign Giant-Cell Synovioma.

C. J. E. WRIGHT (*The British Journal of Surgery*, January, 1951) states that the digits of the hand prove to be much the commonest site of benign giant-cell synoviomata. They occur on the extensor aspect as frequently as on the flexor, those on the extensor aspect probably arising from interphalangeal joint synovium. The average duration of the tumours at the time of the first consultation was two years and seven months, and 40% of the patients gave a history of injury. Benign giant-cell synovioma always originates from synovial membrane, and when arising from a tendon sheath or small joint has a villous structure in its early stages. Eventually, owing to the lack of space in the synovial cavity, the tumour grows outwards as an encapsulated neoplasm. Encapsulation is often absent on the deep aspect, where the tumour blends with its synovial attachments. The villous structure often persists in varying degree; it always does this when the joint space is large, as in the knee. The most characteristic diagnostic feature of the tumour is not the giant cells, but the differentiation into synovial-lined spaces within the tumour substance. Histologically the group includes all gradations from the typical benign form to a more cellular variety of intermediate malignancy, which in turn is closely related to the malignant synovioma. Tumours of the benign type do not metastasize, but in this series they recurred in 44% of cases. Those which recurred were almost invariably of the more cellular variety. Incomplete excision of the synovial attachments of the tumour is probably the most important cause of recurrence. In addition, tiny lobules of tumour tissue only tenuously attached to the main mass may easily be left

behind. Local excision is indicated in every case, whether primary or recurrent, provided this is anatomically possible. The lesion is considered to be truly neoplastic. Blood-cholesterol investigations in 17 selected cases failed to reveal evidence of hypercholesterolæmia. The lipoid accumulations and the siderosis so commonly found in these tumours are considered to be of degenerative or traumatic origin, or both, and purely local phenomena, in part related to the well-known phagocytic powers of the synovial cell.

MORPHOLOGY.

Blood Supply of Cervical Sympathetic Ganglia.

E. L. PATERSON (*Journal of Anatomy*, October, 1950) finds that the superior cervical ganglion receives its blood supply from several sources. These are as follows: (*a*) the ascending pharyngeal artery, the principal and only constant source, the ganglionic arteries arising from its prevertebral branches, its meningeal branch and the parent trunk; (*b*) the superior thyreoid artery, a very common but inconstant source, the extent of its contribution being somewhat variable; (*c*) the inferior thyreoid artery, which commonly provides ganglionic branches either through its ascending cervical branch or by a longitudinal vessel ascending on the sympathetic trunk. Less commonly the occipital and internal carotid arteries provide a supplementary blood supply. The middle cervical ganglion shows variations in the pattern of its ganglionic vessels according to its relation to the loop of the inferior thyreoid artery, its principal and often sole source of supply. The usual arrangement of these vessels in high and low positions of the ganglion is described. In the low position, the thyreo-cervical and costo-cervical trunks may contribute to its arterial supply. The *ganglion intermédiaire* receives branches similar in source and arrangement to those of a low middle cervical ganglion.

Recent Contributions to Study of the Cerebellum.

R. S. SNIDER (*Archives of Neurology and Psychiatry*, August, 1950) reviews the newer contributions to knowledge of the cerebellum and draws particular attention to the following conclusions. Tactile, auditory and visual areas are known to exist within the cerebellum. Motor, tactile, auditory and visual areas in the cerebrum project to these same cerebellar areas, which, in turn, project back on the cerebral areas. It has been established that almost every structure which projects to the cerebellum also receives a projection from it (seldom directly). Certain areas of the cerebellum when properly stimulated produce localized movements and suppression or facilitation of cortically or reflexly induced movement. Cerebellar stimulation can modify cerebral activity. There are single neurological units within the cerebellar cortex which are spontaneously active. It is believed that these units are Purkinje cells and/or the granule-basket cell complexes. It is necessary to abandon the old concepts of a cerebellum which functions as a whole and functions entirely in a proprioceptive sphere. A new concept of function is developed which includes cerebellar action in dampening and in potentiating associated sensory and motor centres alike. The cerebellum thus becomes the "great modulator of neurologic function".

Fate of Nerves of Deciduous Teeth.

A. MOHIUDDIN (*Journal of Anatomy*, July, 1950) has compared, in the cat, nerves of deciduous teeth about to be shed with nerves of sound permanent and deciduous teeth. He states that degenerative changes could always be demonstrated in the axons in the pulp of deciduous teeth in process of shedding. These changes were confined to axons 1μ or more in diameter; finer axons disappeared without preceding changes demonstrable by the silver impregnation methods employed. The onset of degeneration in the nerves preceded evidence of root resorption. Degenerative changes were found only in the axons in the pulp; they were terminal and preterminal in location and did not spread centrally to involve the axons in the dental nerve trunks.

Size of Basal Ganglia of Cerebrum.

P. J. HARMAN AND M. B. CARPENTER (*Journal of Comparative Neurology*, August, 1950) record that a definite alteration of the relative volumes of the various parts of the basal ganglia occurs as the primate scale is ascended towards man. The relatively large caudate nucleus of the early primates decreases, but there is a corresponding increase in the volumes of the putamen of the lenticular nucleus. The ratio of the volumes of the medial and lateral segments of the *globus pallidus* appears relatively constant in all primates. The relative changes in the volumes of the total *globus pallidus* and total caudate-putamen, compared to the relative changes in the volumes of the total basal ganglia, appear rectilinear. The authors state that the quantitative information presented in this communication, when considered in the light of the "law of physiological safety", helps clarify the problem of production of symptoms characteristic of basal ganglia deficiencies in higher primates.

Histochemical Reactions of Normal Teeth.

G. B. WISLOCKI AND R. F. SOGNNAES (*American Journal of Anatomy*, September, 1950) have studied the structure of teeth of different stages of development from man, monkey and the rat, prepared according to a variety of histochemical techniques. The present investigation was undertaken to lay the groundwork of future histochemical investigations of diseased teeth, which are at present under way. The article is illustrated, some figures being in colour.

Sex Difference in Nerve Cell Nuclei.

M. L. BARR *et alii* (*The Anatomical Record*, July, 1950) find that the difference in chromosome content of nerve cells in male and female cats is noticeable in the "resting" nuclei. In the present paper a difference is described in the morphology of the nerve cell nucleus of the cat, according to sex. In the female, a body about 1μ in diameter appears as a small satellite to the large nucleolus in all types of nerve cells examined. In the male, a nucleolar satellite is seldom seen distinctly. There is evidence that male nerve cells contain a nucleolar satellite so small that it lies at the limit of resolution with standard optical equipment. The results of staining with Feulgen and methyl green-pyronin methods indicate that the nucleolar satellite contains desoxyribose nucleic acid, unlike the nucleolus which contains ribose nucleic acid. On the basis of indirect evidence, it is suggested that the nucleolar satellite is a product of the χ chromosome. From the cytogenetic point of view, the satellite may be less intimately related to the nucleolus than the morphological appearance of the resting nucleus would suggest.

Vitamin A and Bone.

N. A. BARNICOT (*Journal of Anatomy*, October, 1950) states that there is now considerable evidence that vitamin *A* plays an important part in the metabolism of bone tissue. It appears that in vitamin *A* deficiency, there is disturbance of the balance of bone deposition and resorption leading to excessive thickness of bone in certain regions, while in overdosage the situation is reversed and the skeleton is weakened. In the present investigation fragments of crystalline vitamin *A* acetate were attached to small pieces of parietal bone cut from ten-day-old mice, and the combination inserted into the cerebral hemisphere of litter-mates. The grafts were removed after seven or fourteen days and were examined either by supravital staining with neutral-red followed by maceration or as histological sections. Well-marked resorption, accompanied by numerous osteoclasts, and often leading to perforation of the bone, was apparent after fourteen days. The significance of the results is discussed in relation to existing knowledge of the skeletal effects on vitamin *A* deficiency and of overdosage with this vitamin.

The Brain of Edinger and Morphology of Ability and Left-Handedness.

W. RIESE AND K. GOLDSTEIN (*Journal of Comparative Neurology*, April, 1950) describe the morphological findings in the brain of Ludwig Edinger, a man who enjoyed great general mental gifts and was pronouncedly left-handed. They state that Edinger's brain is characterized by a remarkable asymmetry—the gyri and sulci on the left side appear to be simpler and more schematic, as it were, than on the right side, and the right hemisphere is five grammes heavier than the left. Although highly endowed in other respects, Edinger was acoustically poorly endowed, so the temporal lobe is structurally much less outstanding. A full description of the brain is given and discussed in relation to the structure of brains of other gifted men. The authors state that what a man actually was and did cannot be stated with certainty from his brain alone, but a study of general cerebral morphology correlated with individual biography can sometimes be very instructive.

Special Abstract.

PHARMACOLOGICAL AND TOXICOLOGICAL ASPECTS OF DDT.

THE Council on Pharmacy and Chemistry of the American Medical Association has authorized publication of a report by the Committee on Pesticides on pharmacological and toxicological aspects of DDT (chlorophenothane of the United States Pharmacopœia).[1] The following is a summary of the main points of the report.

Definition and Properties.

DDT is the abbreviated name for the various mixtures of para, para prime (*p, p'*) and ortho, para prime (*o, p'*) isomers of dichlorodiphenyltrichloroethane, which are used for insecticidal and medicinal purposes. Three grades are recognized: the technical or commercial grade, a partially refined grade and a highly purified grade used in certain special studies. Technical DDT is a soft cream to grey powder with a fruit-like odour. All grades are insoluble in water, but moderately soluble in mineral and vegetable oils and readily soluble in most common organic solvents. For insecticidal use DDT is prepared in the following forms: (i) oil solutions in petroleum or other suitable organic solvents; (ii) emulsion concentrates, which are diluted with water for use; (iii) powders prepared with suitable agents for application as a dust or for use as a spray after mixture with water; (iv) aerosols in suitable oils for dispersion as mist or smoke; (v) coverings included in paints, polishes or waxes. Concentrations in DDT insecticides used vary from 1% to 75%. As an insecticide DDT is used both as a contact and as a stomach poison. It is not a fumigant or repellent, nor has it ovicidal properties. It acts primarily on the nervous system of the insect. Its action is slow; but the facts that small amounts are required and that its action is prolonged increase its value. Its effectiveness varies with the insect, and some species, notably house flies and mosquitoes, have developed a tolerance or resistance to it.

Uses.

A wide variety of insects of economic and public health importance respond to DDT. It has been used extensively in the control of plant and animal pests. It must be applied cautiously to food crops which require treatment after the development of the edible portion of the plant if residues at the time of harvest are to be avoided. It should not be used on dairy cattle or on animals being prepared for slaughter, since there is the danger of accumulation of the substance in the milk and tissues of treated animals. The use of DDT against disease-carrying species of mosquitoes, ticks, fleas and lice, and against flies, roaches, bed-bugs and beetles, has been very successful.

In therapeutics DDT is used as a pediculicide, and in conjunction with benzyl benzoate and ethylaminobenzoate as a pediculicide and scabicide.

Pharmacology.

DDT is a "cerebro-spinal" poison, which acts primarily on the central nervous system in man and higher animals, as contrasted with its apparent peripheral action in insects. The principal systemic effects in higher animals are disturbances of the central nervous system characterized by hyperexcitability, generalized tremors, spastic or flaccid paralysis and convulsions. The cerebellum and the higher part of the motor cortex appear to be the chief sites of action. DDT also sensitizes the myocardium, to the extent that ventricular fibrillation may be induced by sympathetic stimulation either of extrinsic origin, such as the intravenous administration of adrenaline, or from an intrinsic source (sympathin) resulting from sympathetic hyperactivity. It is believed that the production of sympathetic discharges is due to hypothalamic stimulation which, combined with myocardial sensitization, produces ventricular fibrillation. It has been postulated that DDT exerts a physical rather than a chemical action through interference at the lipid surface of the nerve. The action is exerted by DDT itself, and not by a more toxic intermediate metabolite.

Metabolism.—Absorbability is thought to be the principal factor which differentiates the toxicity of DDT in insects from that in man. Under certain circumstances DDT is absorbed through the gastro-intestinal tract, respiratory tract and skin; but DDT in solid form is poorly and irregularly absorbed from the gastro-intestinal tract and practically unabsorbed from the skin. Retention in the respiratory tract depends largely on the size of the particle. Absorption from the gastro-intestinal tract and skin is influenced also by the solvent used; it is favoured by lipoid solvents and by the presence of fat in the intestine. Most animals appear to absorb little or no DDT from the skin unless the compound is in oily solution. Dairy cows are probably an exception to this rule, DDT applied as wettable powders being absorbed through the skin and appearing in body fat and milk. The excretion of DDT is slow and incomplete. Some is excreted through the fæces, urine and bile; the remainder is stored in fat depots, from which it is gradually released, appearing, for example, in the milk of lactating animals. DDT is partly decomposed in the liver to non-toxic metabolites, which are excreted at irregular rates.

Distribution.—DDT is found in all tissues, but mostly in the fat depots of the body. By slow storage an animal may accumulate amounts equivalent to several intravenous lethal doses without showing any obvious signs of poisoning. Of DDT stored, 50% is known to be retained after three months.

Susceptibility.—Various animal species differ widely in susceptibility to poisoning. Increased susceptibility is found in animals lacking large amounts of body fat, fasted animals and young animals. Susceptibility generally decreases with increase in the complexity of the living organism. Among mammals it decreases in roughly the following order: mice, rats, cats, dogs, monkeys, swine, sheep and goats. Birds are especially resistant.

Toxicology.

Although DDT is an inherently toxic material, it has a wide margin of safety when judiciously used, because mammals absorb relatively little of it. Acute poisoning from the absorption of crystalline DDT either through the skin or through the respiratory tract is unlikely, and large oral doses of the undissolved chemical must be ingested to produce symptoms of acute intoxication. DDT in lipoid solvents has a greater tendency to be absorbed from the skin and the gastro-intestinal tract, and is therefore dangerous. The intrinsic toxicity of DDT is about the same for insects and mammals. The lethal dose varies widely with species, with individuals within a species, and with the mode of administration and vehicle used. The range and extent of absorption through body surfaces largely determine the toxic and lethal dosage for a given species. The chronic effects of DDT are similar to those of other halogenated compounds; chronic poisoning may result from prolonged ingestion or exposure to small amounts of DDT. The persistence of these effects depends on the size of the dose and the period of exposure.

Oral Toxicity.—The fatal oral dose of DDT is not known, but it may be about 500 milligrammes per kilogram of body weight for man. This represents about an ounce of the solid material for the average person. A number of deaths attributed to acute DDT intoxication have been reported, but all cases were complicated by the concurrent ingestion of large quantities of solvents, which are capable of producing similar toxic effects. Chronic DDT poisoning may result from ingestion of small amounts of the material over a long time.

Cutaneous Toxicity.—Powdered DDT rarely is toxic or irritating to intact skin, and it does not appear to retard the healing process when contaminating cuts or abrasions. It is not absorbed in this way unless agents which facilitate absorption are present on the skin; such agents would be an oily layer of sebum or greasy solvents. Cutaneous sensitivity resulting from exposure to powdered DDT may be occasionally expected, but this may be due to contaminating compounds. DDT is not considered harmful to the eyes; effects produced by DDT powder splashed into the eye are regarded as the result of mechanical irritation. DDT solution is poisonous. The amounts estimated to be toxic to normal adults on single and frequently spaced multiple exposures are 169 grammes and nine grammes per day respectively. In oil or organic solvents DDT is readily absorbed through the skin with the production of systemic effects. Moderate transient contact with DDT solutions of a low concentration (5% and under) is not dangerous; but prolonged heavy exposure should be avoided. The chief hazard lies in handling concentrated solutions (10% to 25%). Certain solvents and other additives incorporated into DDT preparations are capable of producing irritation of the skin and mucous membranes.

[1] *The Journal of the American Medical Association*, March 16, 1951.

Inhalation Toxicity.—The inhalation of DDT powder offers little hazard because of the large particle size and the relative insolubility of the compound. Certain supposedly inert diluents used in the formulation of DDT wettable powders may irritate the bronchi, producing a persistent cough. In large-scale dusting operations or during exposure to confined conditions where the dust does not move freely on air currents away from the field of operations, respirators should be used. DDT emulsions and certain oil solutions may be readily absorbed by the lungs on inhalation. The concentration of DDT in the atmosphere from the use of the standard 3% DDT aerosol preparation will not produce symptoms of DDT poisoning, even with frequent application, because appreciable concentrations of the insecticide do not stay long in the atmosphere.

Solvents.—Solvents used in DDT aerosols and sprays can cause irritation of the mucous surfaces of the eye and respiratory tract, and may produce intoxication; but little hazard exists with ordinary use.

Pathology.—Information on pathological changes is limited. In acute fatal poisoning significant pathological changes are not likely, although mild to moderate damage to the liver and kidneys may be observed, with perhaps fatty degeneration of the myocardium and occasional hæmorrhages in the adrenals. Terminal pulmonary œdema observed by some investigators is thought by others to be due to solvents used and not to DDT. In more prolonged exposures the pathological changes observed are centrolobular necrosis of the liver, fatty degeneration of the tubular epithelium of the kidneys, focal necrosis of the cardiac and voluntary muscles, and certain central nervous system changes.

Symptoms.—Gross symptoms may be observed in acute DDT poisoning, the severity of which depends on both the dose of DDT and the formulation involved. Twitching of the eyelids is an early sign, which progresses until severe generalized tremors become apparent. The tremors are coarse, beginning in the muscles of the head and neck, and progressing caudally to involve the entire musculature with increasing intensity. They are particularly severe in the extremities, and are elicited by irritation and mechanical stimuli. Death usually results from respiratory failure. Chronic intoxication may be manifested by loss of weight, anorexia, mild anæmia, muscular weakness and tremors that terminate in convulsive seizures, coma and death. The diagnosis of DDT poisoning should be based on the record of exposure and the presence of characteristic neurological manifestations. The presence of DDT can be detected by examination of the urine, but the amount ingested cannot, since degradation products of DDT are not excreted at a uniform rate. Liver function tests may be useful for the measurement of possible liver damage. Abnormal blood findings are usually discovered only in terminal stages of poisoning, and hæmatological examinations are not believed to be of great diagnostic value. Solvents used in the formulation of DDT preparations, particularly kerosene, often produce symptoms which imitate those of acute DDT poisoning; but the signs of solvent intoxication set in promptly, in contrast to a latent period of several hours required for the development of DDT symptoms. This characteristic can be of considerable value in the final diagnosis.

Treatment.—The treatment of acute DDT poisoning is directed towards removing DDT from the alimentary tract and allaying neurological manifestations. Ingested DDT should be removed by gastric lavage followed by the administration of a saline cathartic. Materials which promote absorption, such as oil cathartics or fats in the diet, are to be avoided. Phenobarbital should be given in doses sufficient to control tremors or other nervous symptoms. External stimuli, such as sudden noises or jarring or the administration of adrenaline, which might induce fatal ventricular fibrillation, should be avoided. When chronic poisoning is suspected, symptomatic therapeutic measures which are employed for hepatotoxic substances may be instituted if indicated by liver function tests.

Prophylaxis.

Under the circumstances of ordinary use, DDT is not likely to be harmful; but certain precautions must be observed.

Occupational Precautions.—Persons exposed to large amounts of DDT dusts and powders under confined conditions, or where dust particles are not carried away by free movement of air currents, should wear respirators, and protective clothing should be worn when there is a possibility that greases or oils may contaminate the skin, thereby enhancing the absorption of DDT dusts or powders. Frequent or prolonged exposure to emulsions or solutions of DDT in petroleum oils and organic solvents should be avoided, unless protective clothing, goggles and solvent-resistant gloves are worn. Clothes must be changed promptly if concentrates (10% to 25% or more) are spilled on them. The contaminated skin area which has come in contact with DDT-soaked clothing or spilled DDT concentrates should be washed immediately with soap and water. Concentrates should be mixed in well-ventilated rooms, and fire precautions observed when volatile and inflammable solvents are present. In large-scale spraying or fogging with solutions of 5% or more of DDT, operators should wear respirators and other protecive devices, smoking should be avoided when combustible mixtures are used, greaseless skin lotions should be used on exposed body surfaces when irritant solvents are present in the formulation, and clothes should be changed and the body cleansed after each day's operation.

Household Precautions.—DDT is an effective and useful insecticide, and it is not likely to cause poisoning unless carelessly used. DDT insecticides should not be stored in food cupboards or medicine chests where contamination or mistaken use is possible. Exposed foods, utensils and working areas, and also plants and aquariums, should be covered during household spraying. Children's toys or beds and sickrooms should not be sprayed. Use of oil solutions on household pets should be avoided and DDT powders used only where they cannot be licked off. Intimate skin contact with aerosol discharge should be avoided. The fire hazard of inflammable vehicles should be remembered.

Obituary.

FRANK SANDLAND HONE.

WHEN the medical history of Australia is written, as it must be some day, the name of Frank Sandland Hone will be found among those of men who stood head and shoulders above those of their time because of their vision, enterprise, force of character and example. Some men in medicine are preeminent in one particular sphere; not many have covered so wide a range of activity as Hone, whose death at the ripe age of eighty years was recorded recently in these pages. He was known and loved in his own State of South Australia, where he spent the whole of his professional life; but his influence was felt far beyond its borders. Many who did not know him personally knew his reputation and in matters affecting the whole profession he could not be overlooked. This will be quite clear as the story of his life is unfolded.

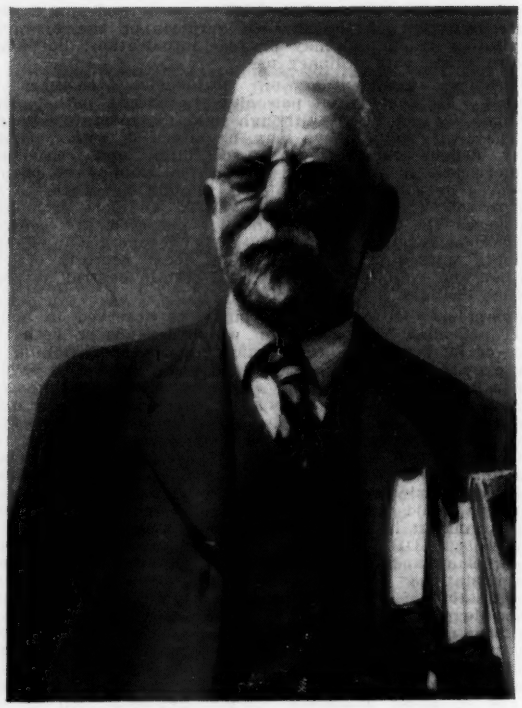
Frank Sandland Hone was born at Mount Gambier, South Australia, on January 7, 1871. His great grandfather was William Hone (1780-1842), author of the famous "Every-day Book", "Table Book" and "Year Book", and in 1819 of "The Political House that Jack Built" with woodcuts by Cruikshank which ran into 54 editions. Lamb's line, "I like you and your book, ingenuous Hone", refers to one of his many works, of which a number were political. The picture by Sir Joshua Reynolds of John Hunter making an anatomical demonstration shows William Hone looking on. Frank Sandland Hone's father came to Australia at the age of eighteen years in 1862 and went into the country. Later he became a Baptist minister. There is no doubt that his early religious associations had a profound influence on Frank Sandland Hone's life. He always took a keen interest in the affairs of the Baptist Church and was at one time chairman of the Baptist Union in South Australia. In the early years of this century he identified himself with the work of the Student Christian Movement. This was one of the many ways in which he tried to help undergraduate students of the University of Adelaide.

Before entering on his undergraduate studies in the medical school, Hone graduated in arts at the University of Adelaide. This was in 1889. In 1894 he qualified in medicine, and after spending a year as resident medical officer at the Adelaide Hospital, he commenced general practice at Morphett Vale towards the end of 1895. In 1903 he moved to Semaphore where he stayed until 1919, when he transferred to North Terrace, Adelaide. At Semaphore he began his preventive medicine activities when he became port health officer. In 1915 he accepted the position of chief quarantine officer for South Australia, and began an association with the Commonwealth Department of Health which was to last for thirty-four years. Writing for *The Review*, the journal of the students of the Adelaide medical school, in the issue of May, 1949, Dr. J. H. L. Cumpston

describes the keenness and the whole-hearted devotion with which Hone carried out the duties connected with the office of chief inspector of quarantine. Dr. Cumpston states that Hone brought to the problems of departmental administration the same clear thinking that he showed in all fields of endeavour. What he did was "a clear refutation of the cherished fiction that a medical man serving a department becomes an uninspired automaton". In 1913 the ideals of preventive medicine were neither so widespread nor so generally accepted as they are today. In an article published in *The Australasian Medical Gazette* in May, 1913, Hone wrote on some problems confronting the South Australian Branch of the British Medical Association. He insisted that nothing should be allowed to interfere with the scientific side of Branch meetings. He continued: "But we have to remember that medicine today is preventive as well as curative, and that as preventive medicine depends largely on legislation, it is as necessary for us to be vitally interested in that as in the scientific side." In July, 1912, he wrote: "It alienates public sympathy from us as an association to see us concerned solely about medical bills and national insurance bills and allowing other bodies to take the lead in approaching the Government in regard to health matters, while we, like Gallio, care for none of these things." He became lecturer in preventive medicine at the University of Adelaide and was able to proclaim his ideals, which he did with the ardour of an evangelist. His breadth of outlook is reflected in an article entitled "Twenty-five Years of Preventive Medicine in Australia", which he contributed by request to the Silver Jubilee Number of this journal in July, 1939. When the Commonwealth Government in 1925 appointed its Royal Commission on Health under the chairmanship of the late George Adlington Syme, Hone was appointed a member. The report of the commission which was published in full in this journal on January 16, 1926, is a document which every medical practitioner who has a live interest in preventive medicine should read. We have it on the opinion of Dr. J. H. L. Cumpston that it was Hone who supplied "the spirit of enterprise" to this commission, "who tried consistently to find a formula for welding Commonwealth and State authority into harmonious unity, and who looked confidently to a future of real efficiency in social medicine". It is important to remember that effect has been given to almost all the recommendations of the commission. When the School of Public Health and Tropical Medicine was established in 1930 at the University of Sydney under the ægis of the Commonwealth Department of Health, Hone became a member of the Advisory Council of the school. He attended meetings of the Council, journeying from Adelaide to Sydney specially for the purpose. In recent years when travelling cannot have been easy for him his friends in Sydney would marvel at his tenacity and vigour. An account of Hone's work in the field of preventive medicine would not be complete without mention of his interest and participation in the Adelaide Hills Children's Health Survey. This is mentioned in the special appreciation by C. C. Jungfer and was discussed in this journal in the issue of July 28, 1945.

As Dr. C. O. F. Rieger states in his appreciation, Frank Sandland Hone began his association with the British Medical Association early in his career. He became a member of the South Australian Branch Council in 1910 as vice-president and occupied the presidential chair in the following year. These were important years in the corporate life of the medical profession in the Commonwealth. The story of the strivings of the Branches for unity, of the formation of the Federal Committee of the British Medical Association in Australia and of the establishment of the Australasian Medical Publishing Company, Limited, in order that the Branches should have one journal has been told on many occasions. Hone took an active part in these happenings. He became one of the South Australian representatives on the Federal Committee and one of the first group of directors of the Australasian Medical Publishing Company, Limited. Both these ventures had to face troublesome times with the outbreak of the first World War in 1914. The Australasian Medical Publishing Company, Limited, had great difficulties in the war years and for a while newsprint had to be used for THE MEDICAL JOURNAL OF AUSTRALIA. But Hone was at one with the late Henry William Armit about the future of the company and of the journal. He stimulated by his mere presence everyone connected with the journal when he visited Sydney for meetings of the directors, and even when he retired from the Board in 1924 and continued as a member of the company he was ready with advice and help whenever he was approached. In the work of the Federal Committee he was most valuable, and it will be recalled that with Sir Henry Newland he drew up what was known as the Hone-Newland report on the cooperation of the medical profession with the Commonwealth Department of Health. (See THE MEDICAL JOURNAL OF AUSTRALIA, March 22, 1924, page 296.) He took an active interest in the sessions of the Australasian Medical Congresses, and when the first session was held at Melbourne under the auspices of the British Medical Association he was president of the Section of Preventive Medicine and Tropical Hygiene.

Of Hone's association with the University of Adelaide, Dr. Helen Mayo has written, and special reference should be made to the work done at the Adelaide Cancer Clinic, of which he was chairman. Of this Professor J. Burton Cleland writes that at the meetings of the clinic every detail was carefully considered and the work was thorough in every way.



In addition to all that has been mentioned about Hone's activities in teaching and administration and in the corporate life of the medical profession attention must be directed to his ability as a clinical observer. In 1922 and 1923 he published in this journal two articles drawing attention to two series of cases resembling typhus fever which had occurred in South Australia. Another paper by him on endemic typhus fever in Australia was published in this journal in 1927. Sir Macfarlane Burnet in *The Review* (Adelaide) in its Diamond Jubilee Edition pays a high tribute to Hone's observations. He states that though in both American and English text-books it is stated that the recognition of a form of typhus not associated with human lice or with a past history of louse-borne typhus was due to Maxcy, Hone had come to the same conclusion as Maxcy some years before the latter's paper was published.

Of Hone's activities in the world of sport Professor Cleland has written. He tells us that, as a young man, Hone with his brother Bert had won the doubles championship at tennis, and that he always kept up a keen interest in all sports activities at the university. "This brought him into close touch with many undergraduates, but apart from this he took a great interest in all medical students who passed through his hands and many kept in close touch with him through their professional lives." It has been said, Professor Cleland avers, that Hone stimulated many by ideas and suggestions to add to medical knowledge and in that way contributed more than in his own writings. This is possibly true, for he had a way of asking a question which was at once a challenge and an invitation. One had to pursue the particular question further and do something about it. He had a generous mind and was gifted with understanding. His sense of humour helped him sometimes

where another might be intolerant, and with his understanding of human nature and human frailties it was impossible for him to be unkind. Hone was devoted to his wife and family. Professor Cleland tells us that "he was much helped in work amongst the poor at Port Adelaide and the Semaphore by his wife, whose unselfish services for the destitute and the unfortunate received recognition by the bestowal of the M.B.E.". Hone himself was decorated by His Majesty the King, who created him a Companion of the Most Distinguished Order of Saint Michael and Saint George. Australia has reason to be proud of such men as Frank Sandland Hone and the medical profession to be thankful for his life and example. He was one of the "biggest" men that Australian medicine in the present century has known, and we do well to remember that the motives which actuated him and the goal that he sought should be those of every medical man and woman.

SIR HENRY NEWLAND writes: It was as a surgical dresser in the third year of my medical course in 1895 that I first met F. S. Hone. At that time he was a resident medical officer at the Adelaide Hospital. His prowess at tennis (he was a member of an outstanding university tennis team) had made him known to me by name only. He began the medical course a little later than was usual. He was one of those who, like C. B. Blackburn, J. A. R. Smith and Violet Plummer a few years later, took on an "arts" or "science" degree before embarking on the study of medicine. After a year as a resident at the Adelaide Hospital Dr. Hone started practice at Morphett Vale, seventeen miles south of Adelaide, and married. About eight years later he sold his practice to my brother Clive and moved to Port Adelaide. There he built up a large practice, and began those medico-political activities which were to prove so fruitful and of such value to his profession, to his State and to the Commonwealth.

Hone had to the end of his days an alert mind. He was a clear thinker, and, like his old and revered teacher, Sir Joseph Verco, believed in method and thoroughness. His strong resonant and persuasive voice coupled with his massive physique attracted attention, interest and trust in what he had to say. He was consequently impressive as a lecturer and also as a member of the Council of the University of Adelaide.

The poor state of his wife's health at an important stage of his career caused him much anxiety, and his devotion led him to abandon for a time medico-political activities which compelled not infrequent visits to the eastern States. I have not the slightest doubt that but for the decree of circumstances he would have enhanced his reputation, high as it became.

I have sometimes thought that Hone had it in him, had he chosen to specialize at an early stage in his career, to achieve great distinction as a medical consultant. But Hone, I am confident, had no regrets. He lived a fine full life, and lived it with a zest. He departed it with tributes showered upon him. To those he held most dear this honour should be an abiding solace.

DR. HELEN MAYO writes: Dr. F. S. Hone's official connexion with the University of Adelaide began when he was appointed lecturer in clinical medicine in 1916. This appointment, which lasted fourteen years, was overlapped by his lectureship in preventive medicine in 1921. This post he held for sixteen years—it was a subject most dear to his heart. In the meantime in 1920 he had been elected as a member of the University Council, and there he continued until his retirement in 1949.

His quality was soon recognized and he was representative of the university on the Sports Association from 1924 till the end of his term on the Council.

In 1926 he became a member of the Finance Committee, that august body which is so powerful in university affairs. In these activities his psychological insight, knowledge of men, instinct for strategy and immense physical and mental drive had full play.

In 1939 he became chairman of the Anti-Cancer Committee, of which body he had been a member since its beginning. This post he retained till the day of his death. During his term of office great developments occurred—a clinical committee, of which he was chairman until 1947, supervised and watched the clinical work of the radium department at the Adelaide Hospital. It was during his chairmanship of the Anti-Cancer Committee that a campaign to raise funds was conducted, the sum reached being over £100,000.

His interest in students extended beyond sport and lectures, and when a students' health committee was formed in 1946 he was a very interested and active member. Previously for nine years Dr. D. R. W. Cowan had conducted, with the help of other doctors, physical examination of medical students, and the results formed a powerful argument for the extension of this benefit to all students. A comprehensive scheme was drawn up by the committee, and when at Dr. Hone's last attendance at the committee it was announced that the Council had decided on compulsory examination of all freshers, he must have felt that his work had not been in vain.

His failing health for the last few years only appeared to strengthen his determination to carry on, and many marvelled at his indomitable courage.

DR. C. O. F. RIEGER, President of the South Australian Branch of the British Medical Association, writes: The profession in South Australia mourns the passing of Dr. F. S. Hone. He was respected by his colleagues alike for the acuity of his mind, undimmed to the end, which enabled him to search out fundamentals of medical and public problems, as well as for the honest straightforward nature of his character. Many of us owe a personal debt of gratitude to him as a teacher, and he was ever ready to assist the young practitioner with sound advice.

He gave much of his time to the advancement of the profession in this State and also in Australia. He was first appointed to the Council of the South Australian Branch of the British Medical Association in July, 1910, as vice-president. In June, 1911, he was elected president for the ensuing twelve months, during which time he advanced the project of the formation of a Federal committee. This coming to pass, he was elected as one of our first two Federal delegates, a position which he filled with distinction until 1920.

Another matter in which he took great interest was the formation of the Australasian Medical Publishing Company, Limited, and he attended as one of the three South Australian members at the first meeting in Sydney on July 16, 1913. He remained a valuable and esteemed member of the company until a few months before his death. He showed a lively interest in the development of a national health service and delivered a paper in November, 1918, advocating the creation of a Federal Ministry of Health with special emphasis on the part it could play in the development of research and preventive medicine.

He was an example to all in his discerning approach to the teaching and practice of medicine and in his appreciation of the charitable nature of our calling and its many responsibilities to humanity, and the profession pays to his memory a sincere tribute of respect.

DR. C. C. JUNGFER writes: I first met the late Dr. F. S. Hone at the Adelaide Hospital in February, 1924. In those days the number of students was small; there were only five of us attached to Dr. Hone's wards. I am sure the other men will remember, as clearly as I do, that first Saturday morning in Verco Ward.

Dr. Hone was an inspired and enthusiastic teacher who believed that the student's first task was to learn to think clearly. He was patient with our lack of medical knowledge, but he would not tolerate muddled thinking. It was typical of his teaching that he was more interested in general principles than in cramming us with detail. This was not reflected in the treatment of his patients where no detail was too small for his attention. As the term progressed we appreciated the breadth of his general knowledge, and we were fascinated by his understanding of the psychological factors involved in any illness.

Our experience was common to that of all students who were fortunate enough to accompany this great teacher on his ward rounds. In our day it was customary for the senior years to come around with us whenever the opportunity arose for them to finish their other duties early. It was then that Dr. Hone was seen at his best; without apparent effort, and with obvious enjoyment, he stimulated and directed discussion between the various groups of students.

It is interesting to reflect that for over sixty years Dr. Hone was associated in some way with medical students. In 1889 he was a student himself, actively participating in the life of the medical school. In his middle years he was a teacher of clinical medicine and lecturer in preventive medicine. Later, after retirement from the staff of the Adelaide Hospital, he worked for the student in many ways, particularly as a member of the University Council. Towards the end of his life, when it seemed that all links with students were broken, they themselves decided to recall him to their midst. In May, 1949, the Adelaide Medical Students' Society published the Diamond Jubilee Edition of *The Review*. This was dedicated to Dr. F. S. Hone, and its pages contain his first extensive biography. Shortly after

this was published Dr. Hone was invited to attend a meeting of the society, and before a very large gathering of students he delivered his last address. Those of us who were privileged to be present felt that Dr. Hone appreciated, as much as anything that had happened in his long life, the way in which he was honoured by the students of the present day.

It is natural that so popular a teacher should be sought as a consultant by his students when they entered practice. When he retired from the Adelaide Hospital in 1930 he expected that the volume of his consultant work would decline, but this was not so. His work for country practitioners increased and I know that many of his happiest memories concerned trips he made to country districts. He was an ideal consultant for country doctors. He understood and liked country people. They were attracted to him by his blunt honesty and, on many occasions, his deeply religious nature was able to bring comfort to simple farm folk who were confronted with problems beyond their understanding.

But his old students came to him not only for medical guidance; many came seeking the advice that only a trusted friend could give. His home was always open to those who wished to discuss their problems with him. They never left without some comfort.

In his private life Dr. Hone was actively interested in church work. In 1935 he was president of the Baptist Union of South Australia. His approach to religion was tolerant and practical. He derived great personal pleasure from his reading of biblical history. I owe him, and his wife, a great deal for many enjoyable fireside discussions on this and many other subjects.

I have not mentioned Dr. Hone's public health activities as these will be dealt with by other writers. In 1939 he interested himself in the Adelaide Hills Children's Health Survey, and for the next ten years he worked continuously on this project. No effort was too much for him. When over seventy years of age he would face a bleak winter's night and a sixty-mile drive to address an audience in the Adelaide Hills. And this was only a small portion of the work he was still doing for preventive medicine.

And so has ended a long life after many years of service in many fields. The Medical School in Adelaide will always rest on some of the foundations he has built. We may ask ourselves what was the secret which he possessed that young men still sought him in his very advanced years. I think the answer is a simple one. It was characteristic of Dr. Hone that, even as an old man, he always looked forward. He was never content unless things were moving ahead. He valued the past for the experience it brought, but it was the dawn on the horizon which attracted him. He had sympathy with the young men who wanted to go forward and he was ready to go with them.

Many of us will always remember one of his favourite quotations because it expressed so well his attitude to life. And, in remembering it, we will hope to retain the outlook he tried so hard to give us.

> New times demand new measures and new men;
> The world advances, and in time outgrows
> The laws that in our fathers' days were best;
> And, doubtless, after us, some purer scheme
> Will be shaped out by wiser men than we,
> Made wiser by the steady growth of truth.

IAN HAMILTON MacGILLIVRAY.

WE are indebted to Dr. Stanley Williamson for the following appreciation of the late Dr. Ian Hamilton MacGillivray.

The sudden death of Dr. Ian Hamilton MacGillivray at his beach home near Murwillumbah on March 22, 1951, marked the passing of one of the State's most gifted and versatile country practitioners.

He was the son of the late Dr. T. K. MacGillivray, of Broken Hill, and received his education at Scotch College, Melbourne, and later graduated M.B., B.S. from the University of Melbourne in 1923. During his student days he gained his college and university blues for rowing. After a period of hospital work he proceeded overseas and gained his Fellowship of the Royal College of Surgeons of Edinburgh. On his return to Australia he joined his father in practice at Broken Hill and carried on with an assistant after his father's death.

In 1939 Ian MacGillivray decided to settle on the north coast of New South Wales, and he purchased a practice at Murwillumbah and later joined the Australian Army Medical Corps. He served with distinction as a surgeon with the rank of major on the hospital ship *Wanganella* during her voyages to Italy, Columbo and south-west Pacific areas. Later he was transferred to 2/5 Australian General Hospital at Morotai. On his return to civilian life in 1946 he built up a very extensive general practice, and his services as a consulting surgeon were availed of by several doctors in Murwillumbah and neighbouring towns. Ian MacGillivray set a very high standard in his professional work and toiled very long hours to cope with the constant and heavy calls on his services.

Apart from his professional work he had many hobbies to occupy his meagre leisure hours and was keenly interested in bird and plant life and photography, in all of which he had a very extensive collection of specimens and notes.

About twelve months prior to his death, he was afflicted with a painful illness, which he bore with calmness and fortitude. His death came suddenly after a heavy day's work.

SIEGFRIED COHN.

WE regret to announce the death of Dr. Siegfried Cohn, which occurred on June 9, 1951, at Maroubra, New South Wales.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Courses for Part I of the M.S., D.G.O., D.L.O. and D.O.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that courses for candidates for Part I examinations for the degree of master of surgery and for diplomas in gynæcology and obstetrics, laryngology and otorhinology, and ophthalmology, will begin on September 3, 1951, for a period of twelve weeks. All lectures and demonstrations will be held at the university in the afternoons only. Details of these courses may be obtained from the office of the Post-Graduate Committee. Early enrolment is essential, and application should be made to the Honorary Director, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 5238, BW 7483.

The Royal Australasian College of Physicians.

SIMS COMMONWEALTH TRAVELLING PROFESSOR, 1951.

Lectures in Sydney.

ATTENTION is drawn to an alteration in the date of the third lecture to be given by Dr. D. M. Dunlop, Sims Commonwealth Travelling Professor for 1951, in Sydney. Owing to electricity zoning the date of this lecture has been put forward one day and will now be held on Tuesday, July 3, 1951, in the Stawell Hall of the College, 145 Macquarie Street, Sydney, at 8.30 p.m. The title of the lecture will be "Some Medical Aspects of Obstetrics and Gynæcology". All members of the medical profession are invited to attend.

Lectures in Melbourne.

The lectures to be given by Dr. Dunlop in Melbourne will be delivered in the Public Lecture Theatre of the University of Melbourne as follows:

Monday, July 9, 8.30 p.m.: "The Status of Therapeutic Dietetics in Medicine" (I).

Thursday, July 12, 8.30 p.m.: "The Status of Therapeutic Dietetics in Medicine" (II).

Monday, July 16, 8.30 p.m.: "The Effect of the Endocrine Glands on the Skin."

All members of the medical profession are invited to attend.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1945, as duly qualified medical practitioners:

Christie, Marjorie Richardson, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Balmain.

Churchward, Sydney Lewis, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Clowes, Gordon Joseph, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Colman, Robin Reuben Simon, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Comins, Thomas Benjamin, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Cooke, Kenneth Henry Stephen, M.B., B.S., 1951 (Univ. Sydney), Royal South Sydney Hospital, Zetland.

Costello, William Thomas, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Cowdery, Richard D'Arcy, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Wallsend.

Cropley, David Oswald, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Cross, Douglas Oakeley, M.B., B.S., 1951 (Univ. Sydney), 43 Gordon Street, Balgowlah.

Deakin, Malcolm James, M.B., B.S., 1951 (Univ. Sydney), 391 Military Road, Mosman.

Degotardi, Colin Boyne, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Cessnock.

Dignam, Phyllis, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Dobell-Brown, David Leslie, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Drummond, John McPherson, M.B., B.S., 1951 (Univ. Sydney), Western Suburbs Hospital, Croydon.

Duggan, John Malcolm, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Duncan, Glen Malcolm, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Dunlop, John Albert Gordon, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Dunlop, William Richard, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Dunn, John Talbot, M.B., B.S., 1951 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.

Edwards, Anthony Wilbraham Tollemache, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Englebrecht, Robert Cecil, M.B., B.S., 1951 (Univ. Sydney), Ryde District Hospital, Eastwood.

Erby, Robert James George, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Cessnock.

Failes, David Geoffrey, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Feinberg, Leonard Henry, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.

Findlay, Wilmet Helena, M.B., B.S., 1951 (Univ. Sydney), Rachel Forster Hospital, Redfern.

Fitzpatrick, Ian Wade, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Ford, Bruce Francis, M.B., B.S., 1951 (Univ. Sydney), Prince Henry Hospital, Little Bay.

Furber, James Gordon, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Gale, Barry Mitchell, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Auburn.

Garner, Ralph Lindsay, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Garrett, William John, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Geeves, Richard Banks, M.B., B.S., 1951 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MAY 26, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	*	..	1	..	..	..	..	..	1
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	..	..	..	..	..	..	..	1	1
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	2(2)	..	1	..	..	..	3
Diphtheria	5(3)	2	3(2)	..	5(5)	..	..	..	15
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	4(4)	8(8)	(1)1	1(1)	..	..	..	14
Encephalitis Lethargica	..	1	..	..	..	..	..	..	1
Erysipelas	*	*	*	3(2)	*	*	..	..	3
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	*	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	..	1	..	..	..	..	..	1
Measles	*	*	*	13(16)	*	*	..	1	14
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	33(12)	7(2)	28(7)	32(19)	1(1)	..	..	..	101
Psittacosis	*	*	*	..	*	*	*	*	..
Puerperal Fever	..	..	..	..	..	*	..	..	..
Rubella(*c*)	*	*	..	*	..	*	..	..	..
Scarlet Fever	10(5)	22(13)	5	3(1)	5(2)	1	..	..	46
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	1	*	*	*	*	*	1
Trachoma	*	*	*	*	*	*	*	*	..
Tuberculosis(*d*)	39(31)	10(3)	13(7)	9(9)	15(10)	5(1)	..	..	91
Typhoid Fever(*e*)	..	..	..	1(1)	1(1)	..	..	..	2
Typhus (Endemic)(*f*)	2	..	6(1)	1(1	1	..	..	..	10
Undulant Fever	..	1(1)	1(1)	..	2(2)	..	..	..	4
Weil's Disease(*g*)	*	*	1	*	*	*	*	*	1
Whooping Cough	*	*	*	2(2)	*	*	..	..	2
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946-1947. Figures in parentheses are those for the metropolitan area.

[2] Figures not available.

[3] Figures incomplete owing to absence of returns from the Northern Territory.

* Not notifiable.

(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Gegg, William Stanley, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Leeton.
Gemenis, Anthony Victor, M.B., B.S., 1951 (Univ. Sydney), Tamworth Base Hospital, Tamworth.
Gershon, Samuel, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Gibson, David Bruce, M.B., B.S., 1951 (Univ. Sydney), Bulli District Hospital, Bulli.
Gibson, William Hector, M.B., B.S., 1951 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.
Gosby, Stanley Noel, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Cessnock.
Gray, Rex Justice John, M.B., B.S., 1951 (Univ. Sydney), Prince Henry Hospital, Little Bay.
Greaves, Collins Louis, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Green, Ruth Helen, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Greenaway, John Moore, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Gunner, Bruce Warren, M.B., B.S., 1951 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.
Gunton, Peter Elliot, M.B., B.S., 1951 (Univ. Sydney), Ryde District Hospital, Eastwood.
Hagan, Brian Elwin, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Halliday, Jonathan Peter, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Hallinan, Geoffrey Michael, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Halloran, Audrey, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.
Harding, Bruce William Ian, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Goulburn.
Harrell, Francis Charles, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.
Harrington, Jeffery Gould, M.B., B.S., 1951 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.
Harris, Henry Thomas Wilfrid, M.B., 1951 (Univ. Sydney), Broken Hill and District Hospital, Broken Hill.
Harrison, Harold Newton, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Hinds, Neville Albert, M.B., B.S., 1951 (Univ. Sydney), St. George Hospital, Kogarah.
Hodgkinson, Anthony Hugh Taylor, M.B., B.S., 1951 (Univ. Sydney), Prince Henry Hospital, Little Bay.
Hooper, James Hamilton, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Parramatta.
Hope, Bertram Kendall, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.
Huber, Felix, M.B., B.S., 1951 (Univ. Sydney), Prince Henry Hospital, Little Bay.
Iceton, Sydney John, M.B., B.S., 1951 (Univ. Sydney), Royal South Sydney Hospital, Zetland.
James, George Robert, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Parramatta.
Jennings, John Colin, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Jessup, Alan, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Johnson, Wilga Miriel, M.B., B.S., 1951 (Univ. Sydney), District Hospital, Lithgow.
Jonas, Siegbert, M.B., B.S., 1951 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.
Jones, Anthony Charles, M.B., B.S., 1951 (Univ. Sydney), Royal South Sydney Hospital, Zetland.
Jones, Bruce Littlewood, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Sydney.
Kalokerinos, Archivides, M.B., B.S., 1951 (Univ. Sydney), Lismore Base Hospital, Lismore.
Keller, Arthur William, M.B., B.S., 1951 (Univ. Sydney), Wallsend District Hospital, Wallsend.
Kellerman, Geoffrey Milton, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Skein, Marie Joyce, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Meldrum, William Arthur, M.B., B.S., 1951 (Univ. Sydney), Lithgow District Hospital, Lithgow.

The undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Jones, David Lewis, M.B., B.S., 1950 (Univ. Adelaide), 12 Giles Street, Toorak Gardens.
Bateman, Peter Patrick, M.B., B.S., 1950 (Univ. Adelaide), 49 Tusmore Avenue, Leabrook.

The undermentioned have been elected members of the South Australian Branch of the British Medical Association:

Muirhead, Mortimer John Croft, M.B., B.S., 1949 (Univ. Adelaide), 14A Gloucester Street, Prospect.
Williamson, David Aubrey, M.B., B.S., 1951 (Univ. Adelaide), "Byways", Crafers.
Phillips, Colin William, M.B., B.S., 1950 (Univ. Adelaide), 3 Ettrick Avenue, Medindie.
Phillips, Pamela Rosemary, M.B., B.S., 1950 (Univ. Adelaide), 3 Ettrick Avenue, Medindie.

Diary for the Month.

JUNE 22.—Queensland Branch, B.M.A.: Council Meeting.
JUNE 26.—New South Wales Branch, B.M.A.: Ethics Committee.
JUNE 27.—South Australian Branch, B.M.A.: Annual Meeting.
JUNE 27.—Victorian Branch, B.M.A.: Council Meeting.
JUNE 28.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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